"*I would have everie man write what he knowes and no more.*"—MONTAIGNE

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EDITORIAL

AN article written by Mr. G. A. Paines, secretary of the Croydon General Hospital Management Committee, in the *Municipal Journal* was reported on January 15 by the *Manchester Guardian*. According to the report Mr. Paines wrote that there is "considerable feeling that the National Health Service is 'fair game' for any claim, however trivial it may be". He suggested that since the start of the service in 1948, £500,000 may have been spent by the Ministry of Health in dealing with claims against hospitals. The *Guardian* quotes again Mr. Paines: "before the National Health Service it was very rare for a hospital to be sued by a patient or next-of-kin for alleged carelessness on the part of any employee, or alleged negligence by Honorary Consultants or nursing staff. But the incidence since then has greatly increased because in many cases the law can be invoked without expense to the litigant . . . ".

So, legislation has cost the Health Service half a million. This enormous figure does not include cases settled out of court, nor does it take into account unsuccessful plaintiffs. Most of the risks to which the flesh is heir, fire, burglary, accidents, damage by storm and tempest, are covered by insurance. Why not also the risk run by all who undergo surgical treatment, anaesthesia, submit themselves to injections of one sort or another, or even to X-ray examinations? Accidents do occur, and severe damage, which may even be irreparable, may follow any of these procedures. Unless the victim can prove negligence he is not likely to get any compensation. An illustration may make the point clearer. A case occurred recently which received considerable interest in the lay press and much comment in medical journals. Following a surgical operation a man found himself irreparably damaged. He brought an action against the doctors concerned and the Regional Hospital Board. The hearing of the case occupied the best part of a fortnight, and the plaintiff lost his case. He appealed and lost the appeal. Evidence was given at the hearing and accepted by the Judge that the accident which accounted for the unfortunate condition of the man occurred once in 10,000 occasions. The patient received no compensation, dragged out a miserable existence for a few years, and then died. Had he been insured, the compensation received would have helped to alleviate his sufferings and provided much-needed assistance for his wife.

Unforeseen accidents from surgical interference are fortunately very rare; the number is not to be compared with the half-million annually caused by speed-intoxicated motorists; the premiums payable to insure against such accidents therefore would be low. If the insurance companies were to underwrite our patients, it would not prevent the patients from bringing actions against Doctors and Hospital Boards. It would, however, certainly reduce the number of such actions and enable juries to come to a conclusion on the evidence and not be influenced by any sympathy they may feel for the litigant. In any case, it would seem that this business is more appropriately in the hands of insurance companies with their staffs skilled in complicated computations than in those of Regional Hospital Boards and Doctors, who cannot have such specialized knowledge. Also the latter would be relieved of much suffering and indignity and would feel free again to choose the anaesthetic or operation best suited to the case, a necessary liberty which, one fears, many may have been shy of taking recently for fear of litigation.

Brit. J. Anaesth. (1955), **27**, 114.

BARBITURATE NARCOSIS IN URAEMIA

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EARLY reports of the use of thiopentone sodium stressed the inadvisability of using the drug in the presence of liver and kidney dysfunction (Goodman and Gilman, 1940; Greene, 1942). This was based on the belief that thiopentone was detoxicated by the liver, and excreted by the kidneys. The role of the liver in the breakdown has been firmly established (Shideman, Kelly and Adams, 1947; Shideman, 1949; Walker and Wyn Parry, 1949; Dundee, 1952) but the breakdown products have little if any narcotic activity (Brodie, Mark, Papper, Lief, Bernstein and Rovenstine, 1950) and only after massive doses of thiopentone does any of the unchanged drug appear in the urine (Mark, Papper, Brodie and Rovenstine, 1949).

Renal tissue is capable of some inactivation of thiopentone (Dorfman and Goldbaum, 1947; Kelly and Shideman, 1949). This must be of little clinical importance since unilateral nephrectomy does not prolong thiopentone narcosis (Schiefly, 1946) and its duration of action is little or unaffected immediately following the removal of both kidneys (Richards, Kueter and Taylor, 1950). However, it has been observed that in uraemic patients anaesthesia could be induced and maintained with very small doses of the barbiturate (Dundee and Richards, 1954).

This paper is a study of the duration of action of medium-acting and short-acting barbiturates in the uraemic dog. A method of establishing a gradually increasing state of uraemia was required for these experiments. It was known from previous work that in dogs the implantation of both ureters into the terminal ileum resulted in such a state. Mann and Bollman (1927) showed that absorption of urea occurred when both ureters were implanted into the duodenum, and that the degree of reabsorption diminished the lower in the intestine the transplantation was performed. Boyce (1951) has shown that the implantation of both ureters into the caecum results in a gradual increase in the blood non-protein-nitrogen (n.p.n.) until the animal dies on the fifteenth to twenty-fourth day. At the time of death the average level of n.p.n. was 106 mg per cent.

PREPARATION

Under general anaesthesia the bladder was divided from the urethra and the divided ends were closed. The blood supply to the bladder and the ureters was preserved intact. An incision about three-

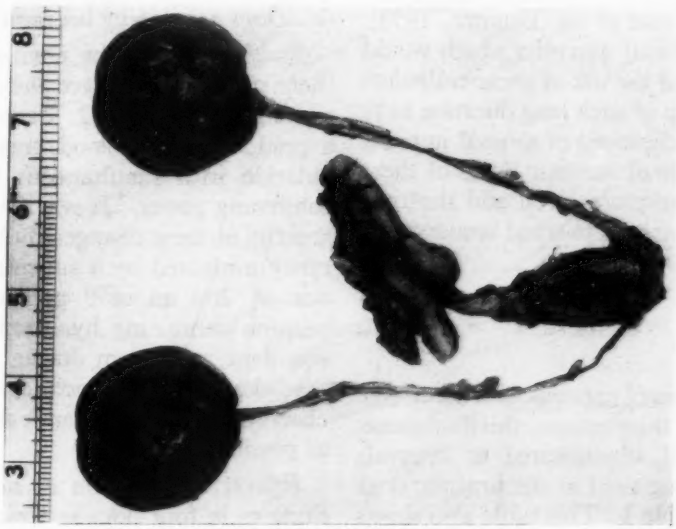

FIG. 1
Post-mortem specimen showing anatomical arrangement of operation described in text.

quarters of an inch in length was made in the fundus of the bladder. The appendix, which is capacious in the dog, was brought out and its tip excised. The open end of the appendix was anastomosed to the hole in the fundus of the bladder; thus all urine went from the bladder, through the anastomosis into the appendix, and thence into the caecum to pass around the large intestine before being discharged at the anus. A post-mortem specimen demonstrating the anatomical arrangement is shown in figure 1.

To establish control data, two mock operations were performed under similar circumstances, in which no anastomosis was made.

METHOD OF OBSERVATION

The duration of action of thiopentone on successive days after operation was studied in detail, and in four animals this was the sole drug used. Other barbiturates used in anaesthetic practice—thialbarbitone (Kemithal), hexobarbitone (Evipan) and thiamylal (Surital)—were studied in less detail. A few observations were made with the basal narcotics, pentobarbitone, quinalbarbitone, and amylobarbitone. The effects of successive injections of thiopentone, thialbarbitone, and thiamylal on non-operated animals were studied as controls.

All drugs were given intravenously by the closed vein technique. Doses of thiopentone ranged from 16 to 19.2 mg/kg. Equipotent amounts of the other members of the same series were used. The average of the times from the end of the injection to (*a*) appearance of corneal reflex, (*b*), spontaneous blinking, (*c*) head raising, (*d*) sitting up, and (*e*) standing unaided, was taken as the duration of narcosis. The reliability of this as a means of measuring the duration of narcosis has been described

elsewhere by one of us (Dundee, 1953). Doses of the basal narcotics which would have permitted the use of these endpoints produced sleep of such long duration as to make these indications of arousal impracticable. Minimal narcotic doses of these drugs were therefore given and the time taken for the animal to stand unaided was used as the endpoint.

RESULTS

(a) *Controls.*

The duration of narcosis with successive injections of thiopentone, thialbarbitone, and thiamylal administered at intervals similar to those used in the uraemic dogs is given in table I. This table also shows the results obtained in the sham operated dogs. It will be seen that there is no cumulative action or tolerance to the barbiturates at the time intervals adopted for observations and that laparotomy alone has no significant effect either on the duration of narcosis or on blood urea.

(b) *Dogs developing uraemia.*

Biochemistry. The changes in blood chemistry which followed the operation are summarized in figure 2. Each dog showed a gradual rise in blood urea and serum chloride with simultaneous fall in CO_2 combining power. It was found that the severity of these changes could be temporarily mitigated by a subcutaneous infusion of 200 ml of 5 per cent dextrose solution containing hyaluronidase. This was done at random during the series so that the effect of each drug could be observed at as wide a range of blood ureas as possible.

Effects on duration of narcosis. The findings in four dogs in which the course of thiopentone anaesthesia had been followed before and after operation until the death of the animals are shown in table II and summarized in figure 3. This figure shows a gradual increase in the duration of narcosis accompanying the increase in blood urea. Figure 4 shows the direct

TABLE I

Blood urea and duration of narcosis in non-operated and sham operated control animals. Numbers in brackets (operated animals) indicate the number of preoperation observations of which the control reading is the average.

	No operation						Laparotomy only			
Dog	209		239		262		163		175	
Barbiturate ...	Thiopentone		Thialbarbitone		Thiamylal		Thiopentone		Thiopentone	
mg/kg	17.3		30		16		13.8		15.8	
Days	Blood urea (mg%)	Duration of narcosis (min)	Blood urea (mg%)	Duration of narcosis (min)	Blood urea (mg%)	Duration of narcosis (min)	Blood urea (mg%)	Duration of narcosis (min)	Blood urea (mg%)	Duration of narcosis (min)
0	23	4.9	28	5.4	18	4.0	26 (7)	4.4	21 (4)	6.8
2nd	20	4.1	31	6.4	18	4.3	42	8.3	26	5.7
4th	20	3.5	24	4.8	21	4.7	30	4.3	22	5.8
7th	35	4.4	32	5.8	17	3.2	40	5.0	20	5.2
9th	26	3.9			26	5.2	37	3.1		
11th	20	4.9	28	4 8	18	4.8	40	4.2	24	4.1
14th	20	4.9	33	5.5	22	4.6	25	4.1	24	4.4
18th	20	4.8				4.3	20	3.4		
21st					21	4.0		4.9		

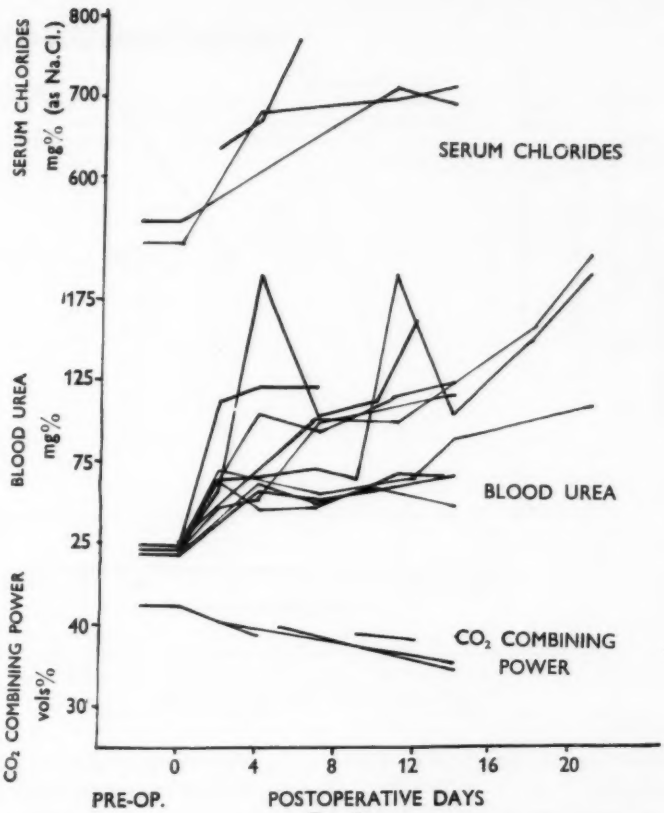

FIG. 2

Composite diagram illustrating changes in blood urea, serum chlorides and CO_2 combining power recorded in twelve dogs after vesico-appendicular anastomosis.

TABLE II

Summary of changes in blood urea and duration of thiopentone narcosis recorded in four dogs, before and at varying intervals following vesico-appendicular anastomosis.

Dog	162		176		208		222		Average	
Dose of Thiopentone in mg	250		150		150		180		182.5	
mg/kg	16.0		15.0		19.2		16.5		16.7	
	Blood urea (mg%)	Duration of narcosis (min)	Blood urea (mg%)	Duration of narcosis (min)	Blood urea (mg%)	Duration of narcosis (min)	Blood urea (mg%)	Duration of narcosis (min)	Blood urea (mg%)	Duration of narcosis (min)
Control	23 2*	10.9	22 3*	7.3	22 10*	10.9	18 3*	7.2	21	9.0
Postop. days										
2nd	66	21.5	74	10.5						
4th	180	39.4	77	15.9	108	45.2	66	15.6	108	29.0
	107	18.1	90	20.5	88	35.7	56	12.0	85	21.6
9th			84	30.1						
11th	126	61.0	184	28.8	132	70.2	58	31.7	127	47.9
14th	177	133.5	107	38.0	150	84.5	43	29.6	119	71.6
18th			152	47.5						
21st			186	48.1						

* The number of control operations.

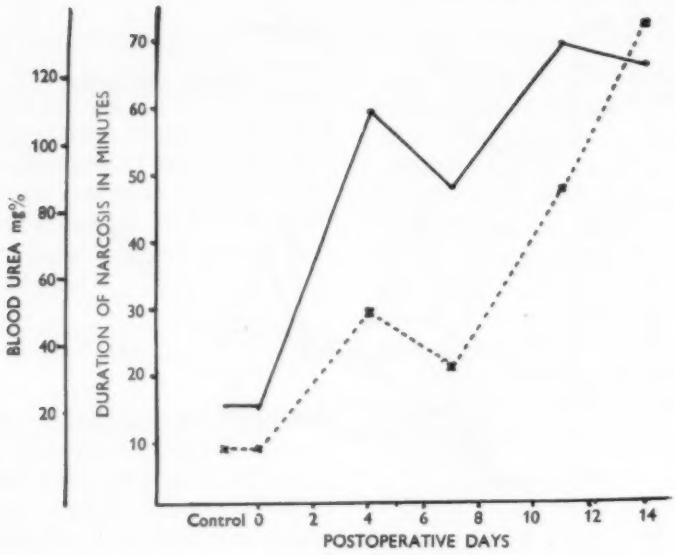

FIG. 3
Average changes in blood urea and duration of action of fixed doses of thiopentone recorded on the 4th, 7th, 11th and 14th day after vesico-appendicular anastomosis in four dogs
——— blood urea. – – – – duration of narcosis.

relationship between the duration of narcosis and blood urea.

Returning to the method of measuring narcosis, the average time taken for each of the signs to appear after injection of the thiopentone is shown in figure 5. The return of the corneal reflex was taken to indicate the end of surgical anaesthesia, while the others were indicative of lessening depths of narcosis. It will be seen that while the duration of surgical anaesthesia is only slightly prolonged the duration of sleep is very markedly prolonged.

Table III summarizes the effect of the operation on the blood urea level, and on the duration of action of the other barbiturates studied. In figure 6 the duration of narcosis is plotted against the postoperative days. Figure 7 shows its relationship to blood urea.

It will be seen that the other barbiturates which were studied behaved in a manner similar to thiopentone. Less reliance can be placed on the results obtained with hexobarbitone as the duration of narcosis produced by the same dose of this drug given under identical conditions varied widely. This unreliability of hexobarbitone is well known and is one of the factors which has led to its almost complete abandonment in modern anaesthesia.

DISCUSSION

Our experimental technique produced a progressively increasing state of urea retention in the animal, but it also produced other biochemical effects. There was a retention of chloride, and a state of acidosis developed in those dogs in which such evidence was sought. Boyce (1951)

TABLE III

Changes recorded in blood urea and duration of narcosis with varying doses of the barbiturates mentioned following vesico-appendicular anastomosis in the dog.

			Control			Postoperative readings		
Barbiturate	mg/kg	Dog	No. of observations	Average blood urea (mg%)	Average duration of narcosis (min)	Post-op. day	Blood urea (mg%)	Average duration of narcosis (min)
Thialbarbitone	31	221	3	28	5.9	14th	123	10.7
	33	223	3	18	7.0	2nd	34	14.8
						11th	102	54.0
	33	228	2	18	8.6	4th	69	21.5
Thiamylal	15	215	3	25	4.1	21st	190	25.4
	16	221	3	25	11.5	4th	44	26.7
	23	223	4	19	8.7	12th	96	26.1
						14th	144	29.1
	23	228	4	19	4.7	2nd	40	13.1
Hexobarbitone	41	221	3	25	18.2	18th	146	31.6
	34	223	4	19	4.5	4th	64	11.0
						7th	85	13.5
						21st	132	15.0
Pentobarbitone	16.4	206	3	20	0.3	2nd	60	15.3
	15	210	2	20	1.2	2nd	45	19.7
	16.4	215	3	19	1.8	4th	80	24.7
Quinalbarbitone	19	228	2	20	13.3	7th	86	24.8
	16.4	210	2	20	1.2	7th	48	14.8
						11th	82	21.0
Amylobarbitone	17	206	2	20	6.8	7th	82	15.3
						14th	88	17.2

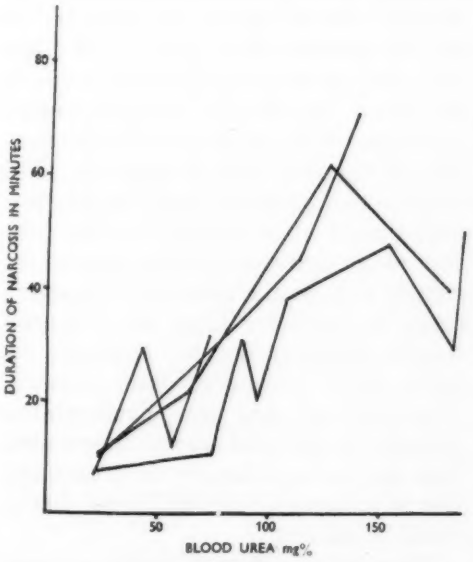

FIG. 4

Relationship between blood urea and duration of thiopentone narcosis in the animals described in the text

noticed a similar development of hyperchloraemic acidosis in his animals.

It seems likely that the biochemical derangements other than the urea retention were responsible for the clinical deterioration and death, because a high level of urea in the blood is not in itself fatal. This is also true in most of the clinical conditions in man which are labelled "uraemia", where nitrogen retention is only one of a number of biochemical derangements.

The results obtained in this investigation show that, in a condition bearing close similarity to uraemia in humans, there is an increased duration of narcosis with short-acting and medium-acting barbiturates in the dog. Furthermore, it would appear that the more severe the uraemia (as judged by the blood urea level), the greater is the increase in the duration of

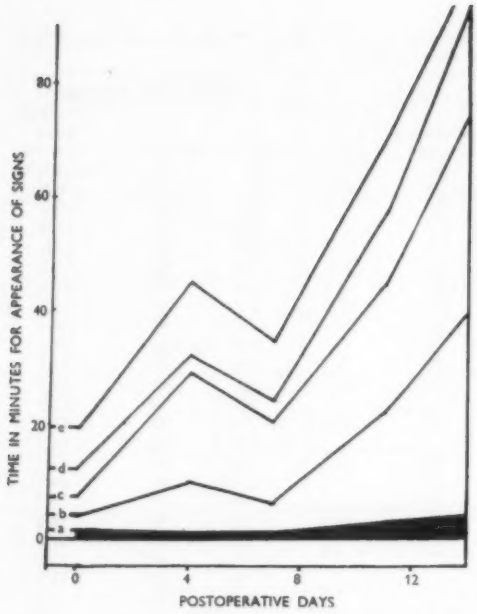

FIG. 5

Average time taken for return of various signs used to determine the duration of thiopentone narcosis in the dog after vesico-appendicular anastomosis.

a. return of corneal reflex. c. head raising.
b. spontaneous blinking. d. sitting up.
e. standing unaided.

The shaded area represents the duration of surgical anaesthesia.

narcosis. This agrees with the clinical observations of Dundee and Richards (1954), who demonstrated extreme sensitivity to thiopentone in uraemic patients. It also substantiates their statement that in humans the total duration of narcosis in the presence of a raised blood urea is increased out of proportion to the actual prolongation of the state of surgical anaesthesia. This correlation of findings is to be expected since, apart from the time taken to reach maximum concentration in body fat, the fate of thiopentone, is similar in man and the dog (Shideman, Gould, Winters, Peterson and Wilner, 1953).

The close relationship between the duration of the narcosis and blood urea was further demonstrated by the following observation.

Dog 267. After operation the blood urea rose as in the other animals, and this was accompanied by an increase in the duration of narcosis with thialbarbitone and thiamylal. On the 14th postoperative day it was noticed that the animal was passing urine per urethra. The blood urea gradually fell, and this was accompanied by a reduction in the duration of narcosis with the two drugs studied. By the 21st day the situation had almost returned to normal (fig. 8).

A urethrogram and systogram taken immediately after the animal was killed demonstrated that the passage for the flow of urine had become re-established (fig. 9). The opaque oil can be seen filling the bladder and overflowing into the caecum and colon.

It is interesting to compare these findings with those of Richards and his coworkers (Richards, Kueter and Taylor, 1950; Richards, Taylor, Davin and Isoshima, 1952; Taylor, Richards and Davin, 1953; Richards, Taylor and Kueter, 1953). They found in animals that *immediately* after bilateral nephrectomy performed under local or light ether anaesthesia, there was no change in the duration of action of thiopentone. If the barbiturate were given 6–24 hours after the operation, there was a rise in the blood non-protein-nitrogen (n.p.n.) accompanied by an increase in the duration of narcosis with thiopentone. This reaction to thiopentone could be produced immediately after nephrectomy by infusion of an artificial n.p.n solution, calculated to raise the blood level to several times the normal. There was a marked species difference in this response, rats being most, and dogs least sensitive. They did not find that hexobarbitone behaved in the same way as thiopentone. This may be explained by the great variation in response to hexobarbitone that we found in the dog.

Blood analysis showed the fall in plasma barbiturate to be the same during the "normal" sleep period in the control and nephrectomized animals. Thereafter,

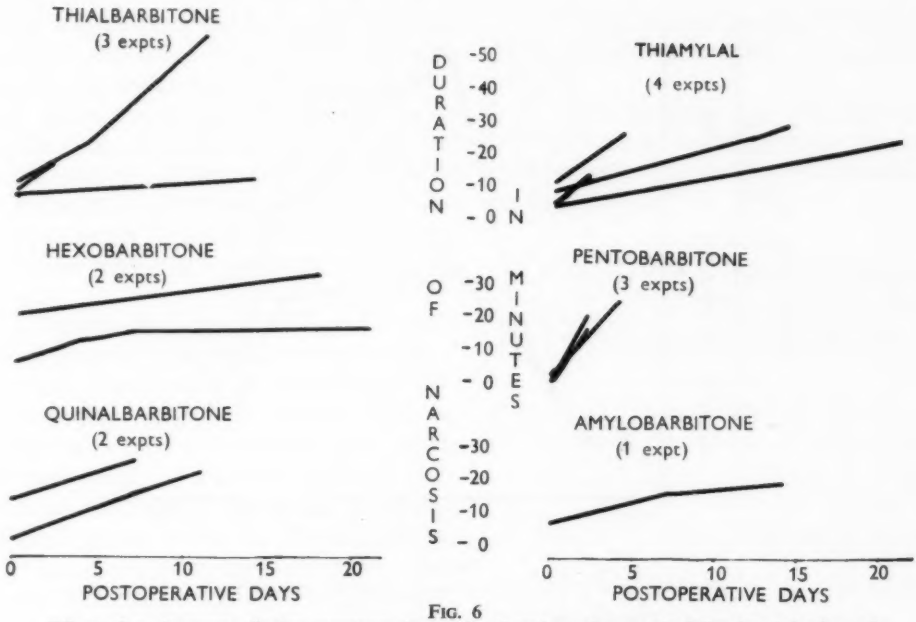

FIG. 6

Effect of vesico-appendicular anastomosis on the duration of narcosis following injection of various barbiturates, doses, etc., of which are given in Table III.

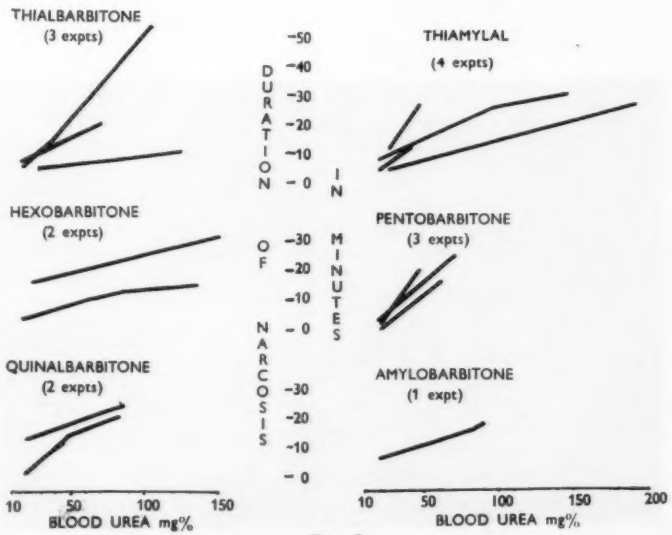

FIG. 7

Relationship of blood urea to duration of action of various barbiturates.

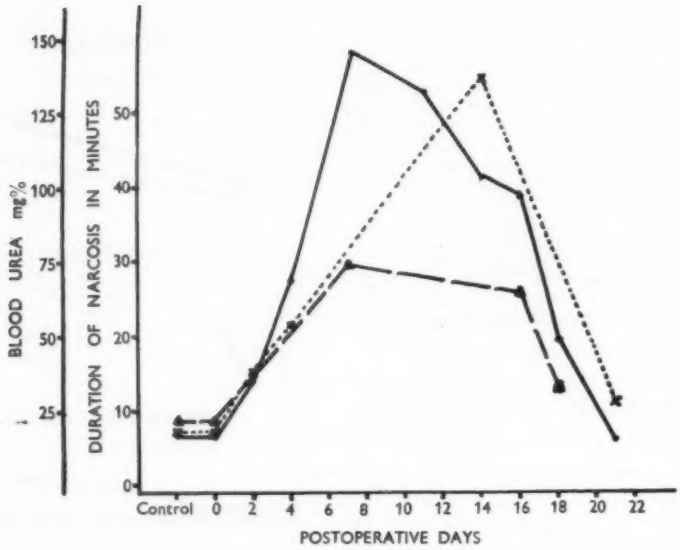

FIG. 8
Findings in dog 267 after vesico-appendicular anastomosis.

——— blood urea.
– – – – duration of action of thialbarbitone 40 mg/kg.
— — — duration of action of thiamylal 17 mg/kg.

FIG. 9
Urethrogram of dog 267, taken on 21st day after operation

there was a slower decline in the operated animals and when these finally regained consciousness the blood thiopentone level had fallen significantly below the one at which these animals wakened during the control sleep. It appeared that not only was the postnephrectomy state associated with a slower degradation of thiopentone but also with a greater sensitivity to the drug.

Richards, Bertcher and Taylor (1952) have shown a similarity between the effect of urea on barbiturate anaesthesia and the potentiating action of glucose and its metabolic products which has been demonstrated by Lamson and his colleagues (Lamson, Greig and Robbins, 1949; Lamson, Greig and Hobdy, 1951a, b). No satisfactory explanation has been offered for this phenomenon but Richards, Bertcher and Taylor have suggested that a change in the permeability of the blood-brain barrier may be the cause of the increased sensitivity to barbiturates.

CONCLUSIONS

In the dog there is a prolongation of duration of narcosis with thiopentone, thialbarbitone, thiamylal barbitone, hexobarbitone, pentobarbitone, amylbarbitone, and quinalbarbitone in a condition closely resembling uraemia in man.

SUMMARY

(1) A method for simulating the clinical picture of uraemia in the dog is described.

(2) The biochemical changes found are discussed.

(3) Narcosis with short-acting and three medium-acting barbiturates is prolonged by uraemia in the dog.

(4) There is a relationship between the degree of uraemia and the prolongation of narcosis.

(5) The application of this finding to man is discussed and suggestions are made as to possible causes of the potentiation of the barbiturates.

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REFERENCES

Boyce, W. H. (1951). *J. Urology*, **65**, 241.
Brodie, B. B. (1952). *Fed. Proc.*, **11**, 632.
—— Bernstein, E., and Mark, L. C. (1952). *J. Pharmacol.*, **105**, 421.
—— Burns, J. J., Mark, L. C., Lief, P. A., Bernstein, E., and Papper, E. M. (1953). *J. Pharmacol.*, **109**, 26.
—— Mark, L. C., Papper, E. M., Lief, P. A., Bernstein, E., and Rovenstine, E. A. (1950). *J. Pharmacol.*, **98**, 85.
Dorfman, A., and Goldbaum, L. R. (1947). *J. Pharmacol.*, **90**, 330.
Dundee, J. W. (1952). *Brit. J. Anaesth.*, **24**, 81.
—— (1953). *Brit. J. Anaesth.*, **25**, 291.
—— Richards, R. K. (1954). *Anesthesiology*, **15**, 333.
Goodman, L., and Gilman, A. (1940). *Pharmacological Basis of Therapeutics*, New York: Macmillan.
Greene, B. A. (1942). *Curr. Res. Anesth.*, **21**, 25.
Kelly, A. R., and Shideman, F. E. (1949). *Fed. Proc.*, **8**, 306.
Lamson, P. D., Greig, M. E., and Robbins, B. H. (1949). *Science*, **110**, 690.
—— —— Hobdy, C. J. (1951a). *Trans. Ass. Amer. Physicians*, **64**, 237.
—— —— —— (1951b). *J. Pharmacol.*, **103**, 460.
Mann, F. C., and Bollman, J. L. (1927). *Proc. Mayo Clin.*, **2**, 134.
Mark, L. C., Papper, E. M., Brodie, B. B., and Rovenstine, E. A. (1949). *N.Y. St. J. Med.*, **49**, 1564.
Richards, R. K., Kueter, K. E., and Taylor, J. D. (1950). *Fed. Proc.*, **9**, 310.
—— Bertcher, E. L., and Taylor, J. D. (1952). *Arch. int. Pharmacodyn.*, **89**, 463.
—— Taylor, J. D., Davin, J. C., and Isoshima, J. (1952). *J. Pharmacol.*, **106**, 411.
—— —— Kueter, K. E. (1953). *J. Pharmacol.*, **108**, 461.
Schiefly, C. H. (1946). *Anesthesiology*, **17**, 263.
Shideman, F. E. (1949). *Anesthesiology*, **10**, 421.
—— Kelly, A. R., and Adams, B. J. (1947). *Pharmacol.*, **91**, 331.
—— Gould, T. C., Winters, W. D., Peterson, R. C., and Wilner, W. K. (1953). *J. Pharmacol.*, **107**, 368.
Taylor, J. D., Richards, R. K., and Davin, J. C. (1953). *Fed. Proc.*, **12**, 371.
Walker, J. M., and Wynn Parry, C. B. (1949). *Brit. J. Pharmacol.*, **4**, 93.

Brit. J. Anaesth. (1955), **27**, 124.

THE RESPONSE OF THE NEWBORN INFANT TO MUSCLE RELAXANTS

BY

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MUSCLE relaxant drugs have been used in Liverpool as part of the anaesthetic technique for operations on newborn infants in over three hundred cases, and it is considered that their use offers three advantages:

(1) They provide a means of effecting and maintaining control of respiration throughout the operation. The importance of this control, which contributes greatly to success in anaesthetizing infants in the first month of life, has been fully described and emphasized by Rees (1950).

(2) The patient is completely relaxed and the work of the surgeon facilitated.

(3) The quantity of toxic anaesthetic agents used is greatly reduced.

If the anaesthetist is to use these drugs to the fullest advantage he must be aware that the response of the newborn infant to these agents differs from the adult. It is the purpose of this paper to show the effects of suxamethonium and d-tubocurarine chloride on the newborn infant, to discuss the possible causes which might produce these effects, and to suggest which relaxant is the most suitable for this type of work.

METHOD

In carrying out these investigations on the neonate it was considered dangerous to inject relaxant drugs without first intubating and obtaining full respiratory control. Accordingly, in all the experiments the infants were intubated without anaesthesia, in accordance with our usual technique, and given a 50 per cent nitrous oxide-oxygen mixture. They were then connected to the apparatus of which figure 1 is a diagrammatic representation. The endotracheal tube was connected, with two T-pieces intervening to a tambour of $1\frac{1}{2}$ inches diameter. One T-piece was used for the inflow of fresh gases, while to the other was attached a fairly long length of narrow rubber tubing, open at the distal end. The internal diameter of the tubes used was at least twice that of the endotracheal tube. This avoided any undue resistance to respiration, but at the same time allowed fluctuations in pressure great enough to affect the diaphragm of the tambour. As fresh gases were being introduced at four times the minute volume of the infant, one may assume that there was no anoxia or carbon dioxide accumulation so long as a normal tidal volume was maintained. The apparatus proved, in practice, satisfactory.

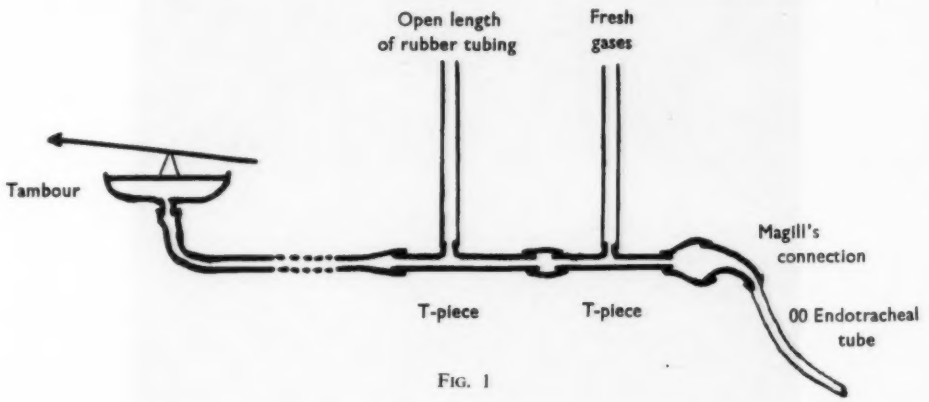

FIG. 1

While the neonate was connected to this apparatus, tracings were taken to allow the amplitude of his normal respirations to be recorded. Varying doses of suxamethonium or d-tubocurarine chloride were then injected through a three-way tap into the saphenous vein. The effect of these injections was either observed or recorded. When suxamethonium was used the period of apnoea so produced was measured; with d-tubocurarine chloride the effect on the amplitude of respiration was recorded.

In order to effect a comparison between the neonate and the adult it is necessary to discuss the dose of suxamethonium that will produce a period of apnoea in the normal adult. Gray (1952) had himself rendered apnoeic by 10 mg of suxamethonium (0.157 mg/kg) for a period of 40 seconds. Mayrhofer (1952) was apnoeic for 50 seconds after 18 mg (approximately 0.314 mg/kg). Thesleff (1952) in his experiments showed that a paralysis of two to three minutes will occur in 95 per cent of cases from doses of suxamethonium of the order of 0.4 mg/kg. In the anaesthetized subject Foldes (1952) has stated that an average of 0.314 mg/kg produced relaxation adequate for intubation.

There seems little doubt that in adult patients with presumably normal pseudocholinesterase levels doses of suxamethonium of 0.4 mg/kg will cause definite periods of apnoea of the order of two or three minutes, while doses of 0.157 mg/kg frequently cause apnoea for shorter periods.

Doses of suxamethonium ranging from 0.314 mg/kg to 0.786 mg/kg were injected into newborn infants.

RESULTS

Effect of Suxamethonium on Neonates.

Two tracings have been selected as typical of the results obtained.

The first (fig. 2) is of neonate Geoffrey, who was seven days old and weighed 6 lb 3 oz (2.8 kg). He was a case of intestinal obstruction occurring four days after an operation for diaphragmatic hernia. His general condition was fair. As indicated (fig. 2) he was given suxamethonium (Scoline) 5 mg/st (0.786 mg/kg). After 20 seconds this caused severe respiratory depression but at no time rendered him

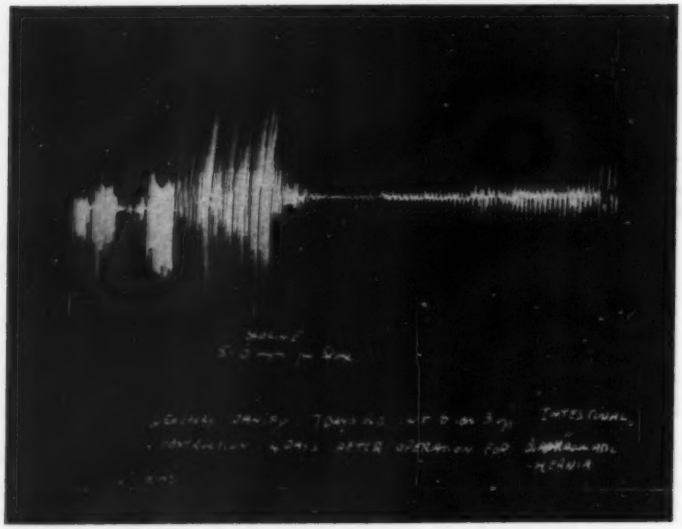

FIG. 2
Kymograph tracing to show effect of suxamethonium (0.786 mg/kg) on respiration of neonate infant Geoffrey D.

apnoeic. His tidal volume then rapidly increased.

The second tracing (fig. 3) is that of neonate Robert who was three days old and weighed 6 lb (2.7 kg). He was a case of intestinal obstruction due to meconium ileus. Suxamethonium 5 mg/st (0.786 mg/kg) was injected. This dose induced a period of apnoea lasting 30 seconds with a rapid return to normal tidal volume.

In a further twenty cases the periods of apnoea were observed. The results are given in table I.

The results show that in fifteen of the cases given 5 mg/st (0.786 mg/kg) the mean duration of apnoea was 50 seconds. The points of significance are that in four of these cases and in two others given slightly smaller doses 0.471 and 0.628 mg/kg, there was no apnoea. In only two cases was the period of apnoea longer than two minutes. When these results are compared with those found in the adult, the resistance of the neonate to the depolarizing agent suxamethonium is clearly shown. The neonate requires at least twice

TABLE I

Case	Suxamethonium mg/st	Suxamethonium mg/kg	Period of apnoea (sec)
1	2	0.314	nil
2	3	0.471	nil
3	3	0.471	5
4	4	0.628	35
5	4	0.628	nil
6	5	0.786	110
7	5	0.786	nil
8	5	0.786	60
9	5	0.786	155
10	5	0.786	5
11	5	0.786	15
12	5	0.786	45
13	5	0.786	nil
14	5	0.786	40
15	5	0.786	140
16	5	0.786	nil
17	5	0.786	60
18	5	0.786	90
19	5	0.786	nil
20	5	0.786	35

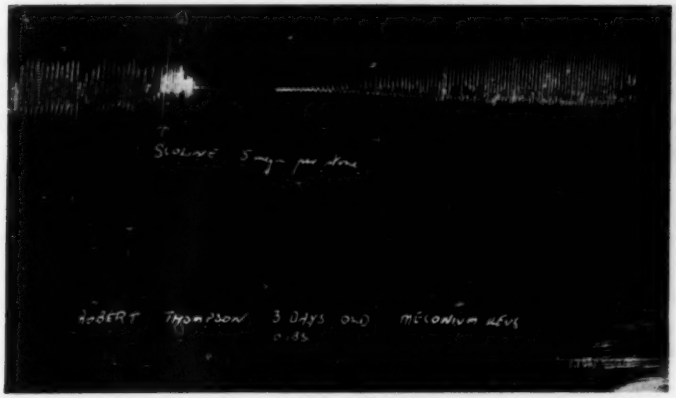

FIG. 3
Kymograph tracing to show effect of suxamethonium (Scoline) (0.786 mg/kg) on the respiration of neonate infant Robert T.

the dose in mg/kg to produce comparable results.

The fundamental differences in the mode of action of competitive and depolarizing agents, and in the mechanism whereby block is produced must necessarily mean that an inverse relationship exists between sensitivity to the drugs causing block in these two diametrically opposed ways. This inverse relationship was shown by Bovet, Depierre, Courvoisier, and de Lestrange (1951), Collier and Macauley (1952) and fully reviewed by Paton (1953). To determine whether this relationship was true for the neonate further observations were made following the injection of small doses of d-tubocurarine chloride.

The effect of the test dose of d-tubocurarine chloride on the neonate.

The effect of 5 mg of d-tubocurarine chloride (0.078 mg/kg in a 10-st man) given as a test dose to the adult prior to the induction of anaesthesia is well known (Gray and Halton, 1948). Normally this dose affects only the muscles most susceptible to the action of d-tubocurarine chloride. It has no noticeable effect on respiration.

Two tracings are shown as typical of the results obtained in neonatal infants. Figure 4 shows the effect upon the respiration of the newborn of a small dose of d-tubocurarine chloride (0.078 mg/kg). This dose, the equivalent of the "test" dose in the adult, produced a very marked decrease in the infant's tidal volume. The neonate was a male, four days old, weighing 5 lb 3 oz (2.4 kg). He was a case of intestinal obstruction due to *volvulus neonatorum* and was in good general condition.

Figure 5 is of neonate John, aged one day and weighing 6 lb 9 oz (2.98 kg). He was a case of high rectal atresia with rectovesical fistula. His general condition was good. At C d-tubocurarine chloride 0.5 mg/st, 0.078 mg/kg) was injected. After three-quarters of a minute the dose

began to affect both the rate and amplitude of his respiration. This effect became very pronounced after 1½ minutes.

These two tracings show the susceptibility of the neonate to the competition blocking agent d-tubocurarine chloride.

DISCUSSION

In making any comparison between the adult and the newborn infant full appreciation of the various factors that might account for any apparent difference is desirable.

It is reasonable to assume that the effect of a relaxant is related to the concentration of the drug at the myoneural junction. A fall in plasma concentration necessarily causes a fall in concentration of the drug in the extracellular fluid and this in turn alters its effect on the motor end-plate.

The weight of plasma to the total body weight bears a similar relationship in the newborn and the adult (Smith, 1946). The neonate, however, has a larger proportion of his total body water in the form of extra-cellular fluid (Fellers, Barnett, Hare and McNamara, 1949).

Muscle mass, the number of motor end-plates, electrolytic balance, and the mechanism available for detoxication may also effect relaxant agents.

The neonate has a higher proportion of its weight in the form of muscle (Shohl, 1939), but it has the same number of muscle fibres and of motor end-plates throughout life (MacCallum, 1898; Le Gros Clarke, 1953).

These physiological differences of the adult and the newborn may cause an alteration in the response to a relaxant agent. If dosage is based upon body weight then a decrease in sensitivity to suxamethonium may be due to a relatively greater dilution of the drug, in the extracellular fluid of the newborn infant. These variables, however, must necessarily affect the response to competitive blocking and depolarizing agents in the same direction. An increased sensitivity to d-tubocurarine chloride together with a decreased sensi-

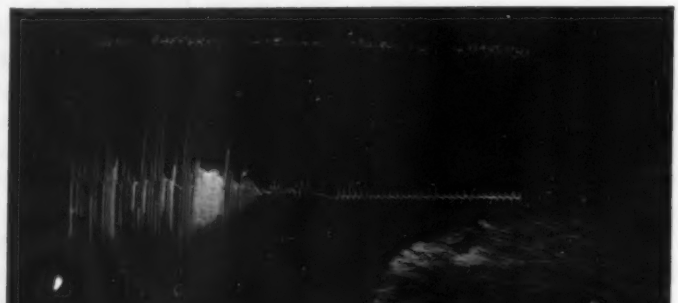

FIG. 4

Kymograph tracing to show effect of a small dose (0.078 mg/kg) of d-tubocurarine chloride on the respiration of neonate Leslie R.

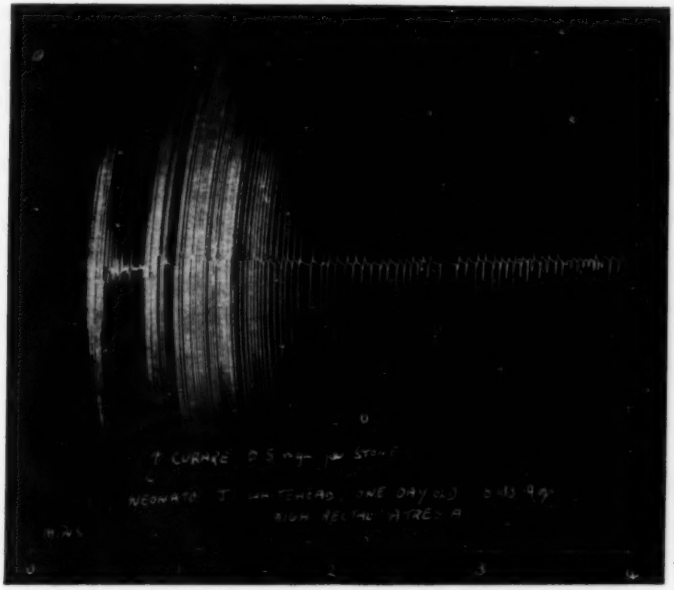

FIG. 5

Kymograph tracing to show effect of a small dose (0.078 mg/kg) of d-tubocurarine chloride on the respiration of neonate John W.

tivity to suxamethonium as found in these observations excludes these factors as aetiological; the change in response in neonates appears to be definitely related to the mode of action of the relaxant concerned.

Alteration in the electrolyte balance can affect the activity of relaxant agents. Potassium is an antagonist to d-tubocurarine chloride. The electrolytic constituents of our newborn surgical cases are, however, within the normal adult range (Ireland, 1953).

Suxamethonium is hydrolyzed by pseudocholinesterase. Low enzyme activity has been reported in newborn infants (Faber, 1943; McCance, Hutchinson, Dean and Jones, 1949). These observations have been confirmed (Stead, 1954). Pseudocholinesterase activity was determined in normal adults, normal newborn infants, and newborn surgical cases. The pseudocholinesterase level of the neonate may be as low as 40 per cent of the normal adult mean. In spite of these low levels for a dose of 5 mg/st (0.786 mg/kg), the period of apnoea has never exceeded, in the first instance, 2 minutes 55 seconds. Low pseudocholinesterase activity is not, therefore, a contraindication to the use of suxamethonium in these cases.

It is possible that a single and overlooked factor might be responsible for either the sensitivity to d-tubocurarine chloride or the resistance to suxamethonium. The fact that the response to both these drugs is altered, together with the

reciprocal relationship between competitive blocking and depolarizing agents, suggests that there may be a physical difference at their common site of action at the motor end-plate.

CONCLUSION

The response of the neonate to doses of d-tubocurarine chloride resembles that of a myasthenic patient. This hypersensitivity indicates the necessity for extreme caution in the administration of d-tubocurarine chloride to neonatal infants. Furthermore, it is doubtful whether a reliable reversal of the action of d-tubocurarine chloride by neostigmine can be obtained in the newborn (Rees, 1951).

Suxamethonium has been used for some 300 neonatal operations in Liverpool, the dosage being 5 mg repeated up to a total dosage of 15–45 mg as required. In spite of lower pseudocholinesterase levels known to exist in such infants there has been no case of prolonged apnoea. The response of the infants to neuromuscular blocking agents leads to the conclusion that from the range of drugs at present available, suxamethonium is the muscle relaxant of preference for use in the anaesthetizing of these infants.

SUMMARY

A method has been devised for recording the respiration of neonatal infants during anaesthesia.

Observations on twenty neonates following the administration of suxamethonium indicated resistance to the paralysant effects of this drug. The neonate appears to require at least twice the dosage to produce an effect comparable to that in adults.

The effect of small doses of d-tubocurarine chloride (0.078 mg/kg) on neonates has been recorded and observed. It is demonstrated that the newborn infant is extremely sensitive to this relaxant showing a myasthenic type of reaction.

Certain aspects of neonatal physiology which might have some bearing on these results have been discussed.

ACKNOWLEDGMENTS

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REFERENCES

Bovet, D., Depierre, F., Courvoisier, S., and de Lestrange, Y. (1951). *Arch. int. Pharmacodyn.*, **80**, 172.
Clarke, Le Gros (1953). Personal communication to T. C. Gray.
Collier, H. O. J., and Macauley, B. (1952). *Brit. J. Pharmacol.*, **7**, 398.
Faber, M. (1943). *Acta. med. scand.*, **114**, 59.
Fellers, F., Barnett, H. L., Hare, K., and McNamara, N. (1949). *Paediatrics*, **3**, 622.
Foldes, F. (1952). *Brit. med. J.*, **1**, 1352.
Gray, P. W. S. (quoted by Evans *et al.*, 1952, *Lancet*, **2**, 682).
Gray, T. C., and Halton, J. (1948). *Brit. med. J.*, **1**, 784.
Ireland, J. T. (1953). Personal communication.
Mavrhofer, O. (1952). *Brit. med. J.*, **1**, 1332.
McCallum, J. B. (1898). *Johns Hopk. Hosp. Bull.*, **9**, 208.
McCance, R. A., Hutchinson, A. V., Dean, R. F. A., and Jones, P. E. H. (1949). *Biochem. J.*, **45**, 493.
Paton, W. D. M. (1953). *Anaesthesia*, **8**, 151.
Rees, J. G. (1950). *Brit. med. J.*, **2**, 1419.
Shohl, A. T. (1939). *Mineral Metabolism*, American Chemical Soc. Monograph Series, No. 82, New York.
Smith, C. (1946). *The Physiology of the Newborn Infant*, Springfield: Thomas.
Stead, A. L. (1954). Unpublished results.
Thesleff, S. (1952). *Acta. physiol. scand.*, **25**, 348.

Brit. J. Anaesth. (1955), **27**, 131.

PHENOTHIAZINE DERIVATIVES IN ANAESTHESIA

A Report on 200 Administrations

BY

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THE benefits to both patient and surgeon conferred by the use of phenothiazine derivatives in anaesthesia are so great that a report on the routine use of these drugs with pethidine as a sole or main anaesthetic agent for adults in general, urological and faciomaxillary surgery may be of interest. Accounts of the pharmacology of chlorpromazine and promethazine have been given by previous writers (Baxter, Bolster and McKechnie, 1954) who have used these drugs to increase the action of anaesthetic drugs and to produce an autonomic block. The use of these phenothiazine derivatives as potentiating agents was abandoned early in this series as it appeared that a more accurate assessment of the patient's condition and post-operative progress could be made if anaesthetic drugs were omitted. Anaesthesia has been produced by the use of chlorpromazine, promethazine and pethidine with a relaxing agent whose action can be counteracted when desired. The advantages of the method described below over other anaesthetic methods previously used have been the smooth and uneventful anaesthesia and the reduced discomfort of the first 36 post-operative hours.

CLINICAL SERIES

The series comprises 200 administrations to 195 patients whose progress was followed until either their discharge home, or to a convalescent or other hospital, or until the end of the third week after operation. The types of operation done are shown in table I. The age range is shown in table II. As a third of the patients were over the age of 60, a fairly high proportion of respiratory and cardio-

TABLE I

Types of operation performed

General surgery		
Thyroidectomy	38	
Gastric operations	31	
Cholecystectomy and common bile duct	26	
Colectomy	6	
Resection of rectum	7	
Laparotomy	3	
Entero-enterostomy	1	
Sacrococcygeal tumour	1	
Hernia	5	
Mastectomy	5	
Neck operations	6	
Parathyroidectomy	2	
Lumbar sympathectomy	3	
Trigeminal section	2	
Removal of rectal polyp	1	
	—	137
Urological surgery		
Kidney operations	14	
Ureteric operations	11	
Cystectomies	10	
Prostatectomies	17	
Oophorectomies	2	
Cystoscopies	2	
Plastic to urethra	1	
	—	57
Faciomaxillary operations		
Excision of maxilla	1	
Bone graft to nose	2	
Impacted molars	2	
Repair of cleft palate	1	
	—	6
		200

TABLE II
Age range

10 to 19 years	9
20 to 29 „	18
30 to 39 „	18
40 to 49 „	38
50 to 59 „	50
60 to 69 „	42
70 to 79 „	21
80 to 84 „	4
	200

TABLE III
Pre-operative complications

Cardiovascular conditions		
Hypertension (Systolic B.P. 170+)	40	
Mitral stenosis	1	
Extrasystoles	4	
Myocardial ischaemia	3	
Right bundle branch block	1	
		49
Chest conditions		
Chronic bronchitis	9	
Bronchiectasis	1	
Asthma	1	
Apical fibrotic tuberculosis with bronchiectasis	1	
		12
Thyrotoxicosis		20
Impaired renal function		4
Jaundice		3
Acute anaemia (haematemesis)		2
Chronic anaemia (Hb 65 per cent)		1
Diabetes		1
Parkinsonism		1

vascular abnormalities was to be expected; 67 patients suffered from one or more of the abnormal conditions listed in table III. The patients were unselected with one exception—that patients undergoing the operation of adrenalectomy were considered unsuitable as the adrenolytic action of these drugs might have had an adverse effect.

METHOD

The anaesthetic technique was based on that advocated by Smith and Fairer (1953). The patients were given promethazine-8-chlortheophyllinate (Avomine) 50 mg. two hours before operation, and pethidine 100 mg. and hyoscine 0.43 mg. one hour before; in elderly patients the hyoscine was replaced by atropine. Half an hour before operation chlorpromazine 50 mg., promethazine 50 mg., and pethidine 100 mg. diluted in saline to 20 ml. were injected intravenously over a period of 5 to 10 minutes. The site of the incision was infiltrated with lignocaine ½ per cent with 1 in 100,000 adrenaline. The patient was then intubated if this was considered advisable. When a relaxant drug was used for intubation 15 to 20 mg. of d-tubocurarine chloride was given unless unusual difficulty in intubation was expected, when suxamethonium (50 mg.) was used. In some cases, particularly the early ones, thiopentone up to 200 mg. or nitrous oxide was used as a supplementary anaesthetic but in 131 cases no supplementary anaesthetic agent has been given. During the operation the original mixture of phenothiazine derivatives and pethidine is repeatedly injected in 5-ml. doses and relaxants given as required. Oxygen on an open circuit or with carbon dioxide absorption with assisted respiration was used when large doses of relaxants made this desirable. Insufficient relaxation for stitching the peritoneum was generally remedied by giving cyclopropane for 2 to 3 minutes rather than giving further relaxant. The total dose of the phenothiazine and pethidine mixture given ranged from 15 ml. to 45 ml. Table IV shows the numbers of cases where supplementary drugs were given.

TABLE IV
Supplementary drugs used

None	34
Relaxant alone	97
Thiopentone alone	10
Nitrous oxide	1
Thiopentone and relaxant	34
Relaxant and nitrous oxide	10
Thiopentone, relaxant and nitrous oxide	6
Incomplete record	8
	200

On return to the ward the patients were nursed on their sides and turned at two-hourly intervals until consciousness had returned. One blanket was used and no artificial heat applied; otherwise no special precautions were taken.

COURSE OF ANAESTHESIA

Effect of premedication. The majority of patients came to the theatre awake but tranquil. A varying degree of post-operative amnesia occurred; some patients, particularly elderly ones, were unaware next day that an operation had been performed, and few patients could remember clearly the conversation immediately preceding the induction of anaesthesia. One patient was distressed after the premedication had been given; he came to the theatre sweating and nauseated with a pulse rate of 40/min. and a blood pressure which had fallen from 140/85 to 80/40 mm. Hg; his pulse rate and blood pressure rose on giving the anaesthetic which ran an uneventful course. The blood pressures of 50 patients were compared before and after the premedication; 28 had a fall of blood pressure. The drop in systolic pressure varied from 10 mm. Hg to 100 mm. Hg; the greatest drop in pressure was from 260/110 to 160/80 mm. Hg. In 11 cases the pressure had risen; the greatest rise in systolic pressure was 70 mm. Hg. In the remaining 11 patients the blood pressure was unchanged by the premedication.

Induction of Anaesthesia. All patients fell asleep either while the injection was being given or within a few minutes. Some degree of analgesia seemed to set in immediately as no objection was made to the infiltration of local anaesthetic being done or an intravenous saline drip being set up even if the patient was still awake.

Intubation. In 70 cases the patient was intubated within 5 to 10 minutes of the injection of the chlorpromazine mixture being given without the use of a relaxant. In 33 of these cases the intubation was easy, in 27 patients intubation was possible but the conditions were not good, and in 10 patients definite difficulty was met. In 98 cases where intubation was done after the injection of 15 to 20 mg. of d-tubocurarine chloride, easy intubation was performed in 36 cases, in 31 cases moderately good conditions were found, and in 21 definite difficulty was encountered. The two series are not comparable as in many dentulous patients a relaxant was given before attempting intubation, whereas in the edentulous patient an attempt was often made before giving a relaxant. The difficulty as a rule was to get adequate exposure of the larynx as the relaxation of the jaw muscles was insufficient. In 9 cases where the facial formation made it obvious that exposure of the larynx would be difficult, suxamethonium 50 mg. was used with excellent results. The impression was formed that intubating conditions were less favourable than those found in thiopentone d-tubocurarine anaesthesia, owing to lack of jaw relaxation even after a relaxant had been given.

Extubation. Although the patients will tolerate a tube without coughing for some hours after the operation is over, it has been the practice to remove the tube immediately on completion of the operation and to insert a pharyngeal airway. Provided the action of any relaxing agent has worn off or been adequately counteracted, the tone of the jaw is good and no trouble with the airway has been met.

Relaxation. The amounts of relaxants given are shown in table V; the 9 cases given suxamethonium for intubation are excluded. The clinical impression received was that the amount of relaxant needed for upper abdominal surgery was similar to that required when the thiopentone, pethidine, nitrous oxide-oxygen sequence was used; the relaxation obtained was of a more complete character and a striking feature has been that the depression of respiration for the degree of abdominal relaxation present was very markedly reduced. It was rarely felt that assisted respiration was essential although the degree of relaxation of the abdominal wall was such that assisted respiration would undoubtedly have been necessary with other techniques. The amount of relaxant used for lower abdominal and kidney exposures was less than was expected. Many cases required no relaxant after the intubation dose. In thyroid surgery, when a relaxant had been used for intubation the degree of relaxation of the neck muscles was strikingly obvious to the surgeon although the patient's respirations remained quite adequate; this was such an advantage in obtaining good access to the structures of the neck that it became the practice to give 15 mg. of d-tubocurarine chloride during the induction of these cases whether it was necessary for intubation or not. Additional relaxation for closing the peritoneum was obtained by giving cyclopropane in 22 cases.

TABLE V

Amounts of relaxants

Type of operation	Amount of relaxant in mg. of d-tubocurarine chloride									
	Nil	10	15	20	25	30	35	40	45	50
Upper abdominal operations	2	—	12	2	12	22	4	5	1	1
Lower abdominal operations	15	4	8	4	6	6	1	1	—	—
Kidney operations	—	1	7	3	1	1	—	—	—	—
Other operations	30	2	28	13	1	—	—	—	—	—

Neostigmine was given in 28 cases. In some patients the dose of neostigmine required was larger than would have been expected for the amount of relaxant given: 4 patients needed 7.5 mg., one 10 mg., and one case 15 mg.

Cardiovascular changes. In 125 cases the pulse was recorded at 5-minute intervals and it was found that tachycardia was common; 94 patients had a pulse rate of 120/min. or more sometime during the operation, a rise of pulse rate immediately after the injection being invariable. Arrhythmia was noticed in 7 patients occurring 15 to 75 minutes after the initial injection; in 4 cases the irregularity lasted 15 minutes or more but in 3 it was observed for only a few minutes. In no case was arrhythmia initiated by intubation.

In 61 patients a blood pressure record was kept at 5-minute intervals throughout the operation. In 59 a drop of the systolic pressure from the immediate pre-anaesthetic reading occurred during the first 15 minutes of the start of the anaesthetic. The maximum and most precipitous fall occurred in hypertensive patients; the greatest fall was from 220/120 mm. Hg to 80/60 mm. Hg and in 11 other patients whose initial pre-anaesthetic systolic reading was over 170 mm. Hg, a drop of

over 70 mm. Hg occured. Intubation generally raised the blood pressure temporarily but the initial fall usually continued for 15 to 30 minutes. In 2 patients the blood pressure rose after the induction of anaesthesia, but in both these patients a considerable fall had already occurred following their premedication. After the initial fall a slow rise took place lasting for about half an hour; in 23 cases the level reached exceeded that of the immediate pre-anaesthetic systolic pressure and in 5 cases the systolic pressure rose over 50 mm. Hg from the pre-anaesthetic level; the greatest rise was from 160/80 mm. Hg to 240/110 mm. Hg. This rise was typically followed by a slow fall the level of which, however, rarely reached as low as the original fall; after 15 to 30 minutes a steady level was generally reached. A sharp drop often followed the administration of neostigmine and the transfer into bed dropped the systolic pressure 10 to 30 mm. Hg.

Surgeons commented on the reduced bleeding which was noticeable even when little or no hypotension was present. This, and the complete absence of sweating were factors which made it possible to reduce considerably the amount of intravenous fluids required during and after the operation.

Respiratory changes. The respiratory rate was slow during the anaesthesia, ranging from 12 to 16 a minute unless a large dose of relaxant had been given, when the rate became quicker and the character of the respiration more jerky. No instance of apnoea occurred with d-tubocurarine; the apnoea following the administration of suxamethonium lasted 1 to 3 minutes. There was no instance of hiccough and reflex laryngeal and bronchial spasm were rare and of short duration. The absence of the laryngeal reflexes to manipulations during thyroidectomy operations was particularly noticeable and responsible for a reduced incidence of post-operative soreness of the throat. The dryness of the upper respiratory tract was a noticeable feature.

POST-OPERATIVE COURSE

Recovery of consciousness. In 100 cases the longest time before a patient answered to his name was 10 hours and the shortest time 1 hour; the average time taken was 4½ hours. Most of the patients having spoken went into a natural sleep again for some hours. As a rule, the patients' recollection of waking was much later than the time the first conversation was held. The quiet recovery period was a noticeable feature of this form of anaesthesia; in 110 patients, 36 had a period of restlessness which lasted only a short time before the patient fell asleep again. Patients showed no evidence of post-operative pain for some hours; in 182 cases, 145 needed no post-operative sedation in the first 24 hours, 31 had morphia gr. 1/6 (10 mg.), 4 had morphia gr. ¼ (16 mg.), and 2 morphia gr. 1/3 (20 mg.). A certain number of patients required morphia on the evening of the day following operation, and it would seem from conversation with patients who had experienced previous abdominal operations that a period of post-operative analgesia lasting approximately 36 hours exists. The patients were markedly more cheerful and alert once consciousness had returned than is usual after a major operation. Two patients

complained of dizziness on the following day.

Temperature changes. Most patients returned to bed with a subnormal axillary temperature as shown in table VI. In some cases the subnormal temperature was followed by an immediate rise in temperature which might last 1–2 days as shown in table VII. Two patients had a rigor in the first 24 hours following a prostatectomy operation and 6 patients ran temperatures ranging from 99° to 101°F (37.2° to 38.3° C) for 3 to 7 days for no apparent reason. In 100 patients, 65 awoke before the temperature had reached a normal level.

TABLE VI

Temperature on return to ward	No.	Time to become normal	Average time
Normal	6	—	—
97°F.	20	1–12 hours	6.4 hours
96°F.	42	2–12 ,,	6.8 ,,
95°F.	30	4–21 ,,	7.0 ,,
94°F. or less	5	4– 8 ,,	7.6 ,,
	103		

TABLE VII

Post-operative changes (103 patients)

Post-operative temperature	Day of operation	1st post-operative day	2nd post-operative day
99°F.	27	30	16
100°F.	21	22	11
101°F.	5	9	—
102°F.	1	1	—

Post-operative vomiting. In 148 cases where the vomiting in the first 24 hours was recorded, 19 patients vomited once, 4 patients vomited twice, 2 three times, and 1 patient repeatedly. Patients who had the stomach aspirated through a Ryle's tube were excluded from these records. Three patients who had had severe post-operative vomiting after previous anaesthetics were free from vomiting after this one. In some patients vomiting would occur on the night of the first and second day after operation, again as though the anti-emetic effect of the drugs wears off in 36 hours.

Cardiovascular changes. The pulse rate stayed remarkably steady after operation; in 20 per cent of cases it rose in rate as the temperature rose and then remained at a steady level; in the other 80 per cent it was at a steady rate regardless of blood pressure and temperature changes. The rate was between 80 and 100/min. in 68 patients, between 100 and 120/min. in 24 patients, and over 120/min. in 8 patients of the 102 patients whose pulse and blood pressure readings were recorded for the first 12 hours after operation. The majority of patients returned to bed with some degree of hypotension. Thirty-five patients of the 102 had a drop of more than 70 mm Hg from their pre-operative systolic level; in 33 of these patients the blood pressure rose to within 70 mm. Hg of their normal pressure within 6 hours, but 2 took 12 hours to reach this level. In 49 of the 102 patients the systolic pressure had not reached the normal level in 12 hours. In most patients the blood pressure rose steadily, though at varying rates, but in 4 patients it fell for the first 4 hours before starting to rise. In 3 patients the pressure rose to above its pre-operative level for a short time. The greatest fall was from 240/110 to 70/? mm. Hg; this patient, an elderly woman who had had a hemicolectomy done, had a blood pressure of 110/60 mm. Hg at the end of the first 6 hours and 140/60 mm. Hg at the end of the next 6 hours. Hypertensive patients had the greatest degree of hypotension and took the longest time to return to their normal reading.

POST-OPERATIVE COMPLICATIONS

There were no deaths in the series.

Cardiovascular complications. One woman of 62 years of age with hypertension (B.P. 250/150) developed auricular fibrillation 2 days after a cholecystectomy had been done; this persisted for 48 hours, after which she made a good recovery.

Chest complications. Three patients developed atelectasis, 1 bilateral and the others affecting one lobe; none were seriously ill and all recovered within a few days. Seven patients had a cough with sputum, a rise in temperature and moist sounds in the chest; all were satisfactory within a few days. It was noticeable that the patients coughed easily and without pain and could co-operate with the physiotherapists without discomfort. Several patients who might have been expected to develop chest complications did not do so, and it was felt that chest complications were less troublesome than might have been anticipated. The deep respiration, lack of bronchospasm and the dryness of the upper respiratory tract and the relief of post-operative pain were all factors which might have influenced the reduction of respiratory complications, although it might have been thought that the prolonged period of unconsciousness after operation would predispose to them. Two outstanding examples of patients in whom respiratory trouble might have been anticipated were a woman with bronchiectasis who had a cholecystectomy done, and a man with apical fibrotic tuberculosis associated with bronchiectasis who had a gastrectomy performed. Both were able to cough easily and bring up their normal amount of sputum from the first day. One man developed a pleural effusion and an effusion into the knee joint following a partial nephrectomy for renal tuberculosis; he recovered sufficiently to undergo a transplant of ureter a few weeks later which was followed by no complications. Two patients had pulmonary infarctions, one on the 10th day after a gastrectomy and the other on the 4th day after a radical mastectomy; neither was seriously ill and both made a good recovery.

Gastro-intestinal complications. Two patients had acute dilatation of the stomach; one following an emergency gastrectomy for a perforated duodenal ulcer and the other following a cholecystectomy in a patient with a marked degree of pyloric spasm; both recovered on gastric suction. On the whole complaints of intestinal flatulence and distension were uncommon and no case of paralytic ileus occurred. The 3 patients with jaundice all made an uneventful recovery.

Mental complications. An elderly woman was confused mentally on the first day after a lumbar sympathectomy for senile gangrene; she became normal after two restless nights. Another woman, aged 76, suffered from mental confusion for the first 2 post-operative days after a mastectomy, but was normal on discharge.

Urological complications. A boy required catheterization after the removal of a sacrococcygeal tumour. Two patients had a rigor after prostatectomy.

Surgical complications. One patient required laparotomy for intra-peritoneal haemorrhage which occurred 20 hours after a gastrectomy. Another had a resuture of wound on the 10th post-operative day and a third a prostatic bed haemorrhage on the 7th day.

COMMENTS

The use of these drugs as anaesthetic agents is considered to be beneficial for the following reasons:

1. The patient has a pain-free post-operative period for approximately 36 hours. The incidence of post-operative vomiting appears to be reduced, the immediate post-operative period is free from anxiety, and the nursing attention is reduced to a minimum. Elderly patients and patients suffering from chest conditions benefit especially from this anaesthesia. Some patients who had experienced major operations under other forms of anaesthesia were very appreciative of the freedom from post-operative pain and discomfort.

2. Good operating conditions are produced with safety to the patient; no crisis or periods of anxiety arose during the induction of anaesthesia or the course of operation.

3. Reduction of bleeding and sweating reduces the need for the intravenous administration of fluids except to replace the blood lost at operation, which is minimal.

4. The method is considered to be particularly suitable for cases suffering from thyrotoxicosis, as these patients are markedly calmer and more free from discomfort than those operated upon under other forms of anaesthesia. The lack of bleeding and easy exposure of the gland reduces the incidence of post-operative sore throats and huskiness.

ACKNOWLEDGMENTS

I should like to thank Mr. George Armitage, Mr. Leslie N. Pyrah, Mr. Michael Oldfield, and other surgeons of the United Leeds Hospitals, under whose care the majority of these patients were, for their interest and helpful comments; also the sisters and nursing staff of the Leeds General Infirmary for their valuable help in the keeping of records.

REFERENCES

Baxter, R. W., Bolster, J. A., and McKechnie, S. (1954). *Anaesthesia*, **9**, 79.

Smith, A. J., and Fairer, J. G. (1953). *Brit. med. J.*, **2**, 1247.

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OUABAIN IN THE TREATMENT OF SHOCK

BY

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AND

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THE use of ouabain in the treatment of shock was first reported by Sankey and Crawford (1950), acting upon a suggestion by Wiggers (1947) that cardiac stimulants might reverse circulatory failure in cases of shock in which transfusion fails.

We have been using ouabain for this purpose for the past three years. This paper reports the results of the administration of ouabain in 73 cases.

PHARMACOLOGY

Ouabain (strophanthin G) is a cardiac glycoside obtained from the seeds of strophanthus gratus; it consists of small colourless crystals, or a white crystalline powder with a bitter taste. It is soluble in water (1 part in 100) and in dehydrated alcohol; and may be sterilized by heating in an autoclave or by filtration (Martindale, 1952).

"Ouabaine Arnaud", the preparation which we use, contains 0.25 mg. ouabain in 1 ml. of water suitable for intravenous injection.

Ouabain has an action similar to strophanthin K, but it is twice as potent. It has a rapid action, is quickly excreted and its effect is short. It is said to be dangerous to give ouabain to patients who have been digitalized during the previous 14 days.

The intravenous dose of ouabain is 0.25–0.5 mg. The maximum permitted dose in 24 hours varies between 0.25 mg. and 5 mg. according to various authorities.

INDICATIONS FOR THE USE OF OUABAIN

Myocardial depression is one of many possible factors involved in the mechanism of surgical shock. It may exist even under otherwise normal circulatory conditions, the heart being near the limit of its reserve, and, when other factors are added, shock and circulatory failure may quickly follow. We believe that the myocardial stimulating properties of ouabain are of value in the following circumstances:

(1) In shock, to aid the effect of volume replacement, before, during, and after operation.

(2) To restore the blood pressure without volume replacement (i.e. without coincident transfusion), especially where there is peripheral vasoconstriction or tachycardia, and when vasopressor drugs might thus be contra-indicated.

(3) In patients with hypertension when there is a sudden fall in blood pressure due to induction of anaesthesia, peritoneal stimulation, etc.

(4) To correct the circulatory depression caused by altering the patient's position, etc.

(5) Prophylactically in cases where indications (3) and (4) may be expected to occur.

(6) In certain cases of cardiac arrhythmia, especially when associated with a falling blood pressure or venous engorgement.

RESULTS

Ouabain (0.25 mg.) has been given intravenously to 73 patients during anaesthesia for a variety of surgical procedures, the majority of which were major intra-abdominal or abdominothoracic operations. In addition, it has been used on a number of occasions with benefit during pre- or post-operative resuscitation. Only the former group is analysed here, as the details recorded were more precise.

Total number of administrations = 100 (73 *patients*).

Of these, the circulatory state showed improvement in 79, no change in 7, and continued deterioration in 10. (Details were insufficient in 4.)

On 80 occasions when ouabain was given, full details were recorded upon the anaesthetic charts, and accurate analysis was possible. The following study was made in these cases. The blood pressure before the administration of ouabain, and for the two successive readings after, was noted, and the mean blood pressure calculated (mean B.P. = diastolic B.P. + ⅓ pulse pressure) for each reading. The mean blood pressure before the administration and that closest to 10 minutes after were taken for comparison. This time was chosen as that at which the maximum effect of ouabain on arterial blood pressure is to be expected (McMichael, 1950), though the cardiac output might be expected to be increased later, even if the blood pressure had again fallen.

On this basis:

EFFECT OF OUABAIN ON MEAN BLOOD PRESSURE

Rise	67 (84 per cent)
Fall	9 (11 per cent)
No change	4 (5 per cent)
Total	80 (100 per cent)

Of the 67 *cases showing a rise in mean blood pressure*:

Mean percentage rise = 32.4; standard deviation of the mean = ±29.1; standard error = 3.5.

Of these 67 cases showing a rise in the mean blood pressure after the administration of ouabain, there were ten occasions in which fluid replacement was not given.

Of the 9 *cases showing a fall in mean blood pressure*:

Four patients were still bleeding, and improved with adequate blood replacement.

Five patients improved with a further injection of ouabain (0.25 mg.), suggesting that the initial dose was inadequate.

In five cases, the fall in the mean blood pressure after the administration of ouabain was also associated with the induction of anaesthesia, movement of the patient into the theatre, or the administration of depressant drugs, such as pethidine.

Of the 4 *cases showing no change in mean blood pressure*:

Two cases showed a rise in systolic blood pressure with increase in pulse pressure; one showed a transient rise in mean blood pressure which had passed off at 10 minutes, and in the fourth case the final blood pressure reading was taken too soon after the administration of ouabain for the full effect to have been achieved.

ILLUSTRATIVE CASE REPORTS

A. *Use of ouabain to aid moderate blood volume replacement in shock, and to avoid circulatory depression consequent upon anaesthesia and operative manipulation.*

Case I. B.C. Male, 70 (fig. 1).

Normal B.P. 185/90 mm. Hg. Perforated peptic ulcer of 20 hours duration. Shocked. B.P. 100/80. Dextran 500 ml., blood 250 ml. and ouabain 0.25 mg., given intravenously 30 minutes before arrival in theatre. On arrival B.P. 120/80, pulse 100. Ouabain 0.25 mg. intravenously at O. Oxygen inhalation for 15 minutes before induction of anaesthesia. Further improvement in blood pressure to 150/100. Premedication, atropine 1/100 grain (0.65 mg.). Induction with nitrous oxide, oxygen, ether; intubation; maintenance with cyclopropane, oxygen; relaxation by 0.1 per cent suxamethonium drip. Blood pressure level maintained well during operation.

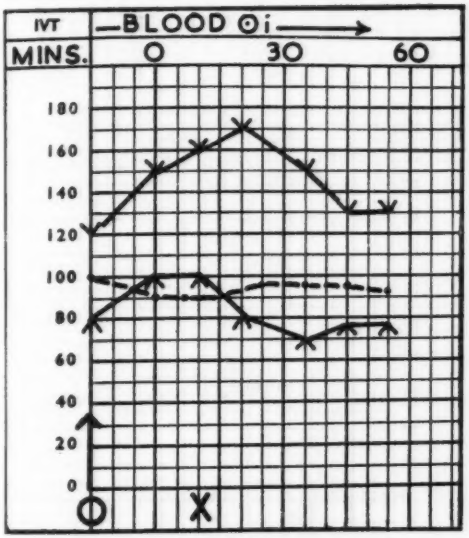

FIG. 1

B. *Marked effect of ouabain following moderate rise in blood pressure gained by transfusion.*

Case II. A.M. Female, 80 (fig. 2).

Pre-operative blood pressure 170/110. Partial gastrectomy for haematemesis, bleeding continuing and patient receiving blood. Premedication: morphine 1/6 grain (10 mg.), atropine 1/120 grain (0.5 mg.). On arrival in theatre, blood pressure 110/60. Induction with nitrous oxide, chloroform, ether; intubation; maintenance with cyclopropane and oxygen. Relaxation with d-tubocurarine-chloride. Progressive fall in blood pressure after induction to 90/50. At 25 minutes 250 ml. of blood given rapidly; blood pressure rose to 120/80, blood then given more slowly. Ouabain 0.25 mg. at O. Marked rise in blood pressure to 160/80 in 10 minutes.

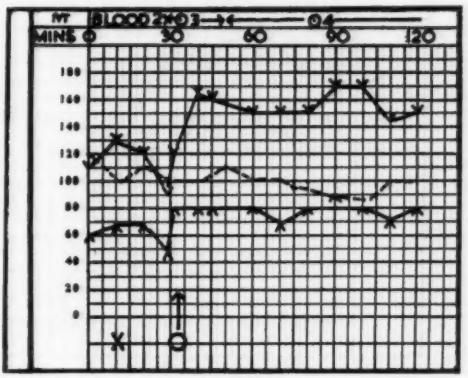

FIG. 2

C. *Use of ouabain to aid intravenous transfusion after massive blood loss.*

Case III. H.G. Female, 62 (fig. 3).

Carcinoma of splenic flexure; excision and anastomosis, splenectomy. Premedication, pethidine, 75 mg., atropine 1/120 grain (0.5 mg.). Induction with thiopentone and suxamethonium; intubation; maintenance with cyclopropane-oxygen, relaxation by 0.1 per cent suxamethonium drip. Severe haemorrhage at 75 and 150 minutes. Blood pressure fell to unrecordable levels. Ouabain 0.25 mg. at O, with blood given rapidly. Excellent response on each occasion.

D. *Use of ouabain alone to correct blood pressure fall due to induction of anaesthesia, abdominal manipulation, etc.*

Case IV. A.H. Male, 77 (fig. 4).

Biliary fistula—excision of fistula, cholecystectomy, choledochostomy. Premedication, morphine 1/8 grain (8 mg.), atropine 1/120 grain (0.5 mg.). Induction with nitrous oxide, chloroform, ether; intubation; maintenance with cyclopropane and oxygen; relaxation with 0.1 per cent suxamethonium drip. Severe fall in blood pressure with early intra-abdominal exploration. Ouabain 0.25 mg. given at O. B.P. rise to 130/70.

Case V. A.C. Male, 47 (fig. 5).

Gastric ulcer, partial gastrectomy. Premedication, morphine 1/6 grain (10 mg.), atropine 1/120 grain (0.5 mg.). Induction with thiopentone 300 mg., suxamethonium 40 mg.; intubation; maintenance with nitrous oxide, cyclopropane and oxygen; relaxation with 0.1 per cent suxamethonium drip. Fall in blood pressure to 70/50 mm.Hg after induction and initial abdominal exploration. Ouabain 0.25 mg. at O. Blood pressure restored to initial level in 10 minutes without other supportive therapy.

NOTE: In all the illustrations time is shown in minutes from beginning of anaesthesia:
X=Incision; O=ouabain 0.25 mg. I.V.

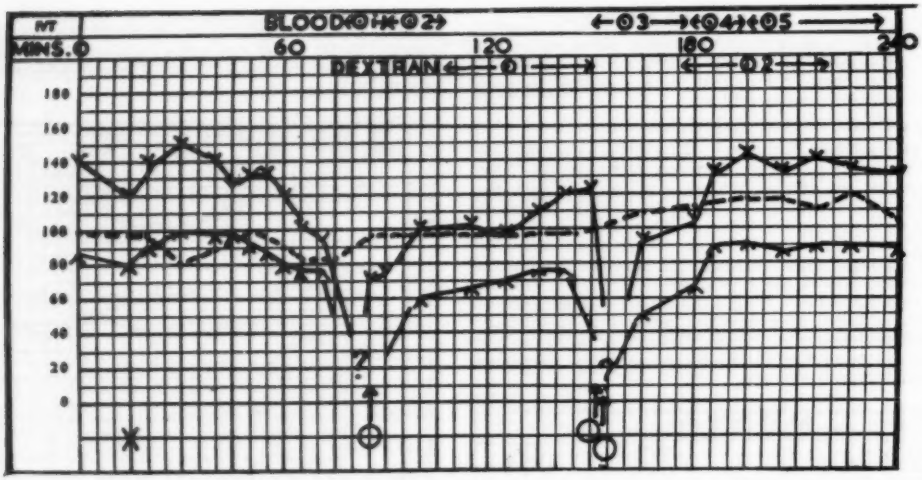

FIG. 3

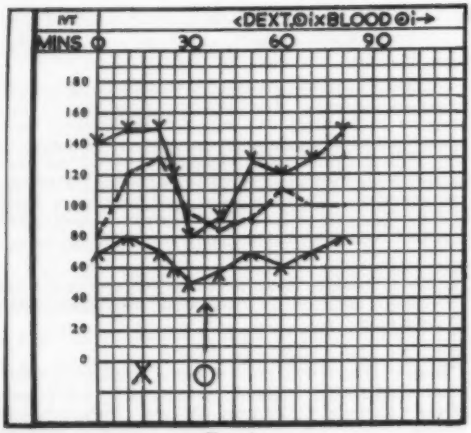

FIG. 4

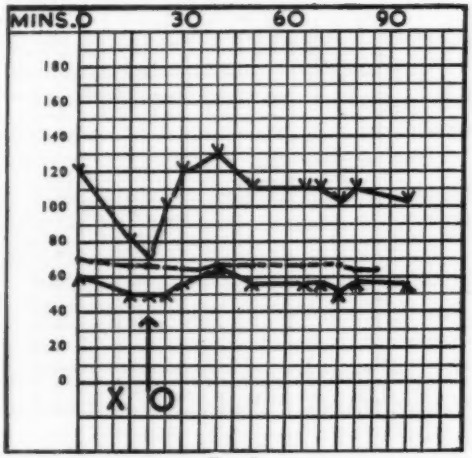

FIG. 5

E. *Occasional transient action of ouabain upon blood pressure in shock.*

Case VI. M.C. Female, 74 (fig. 6).

Obstructive jaundice, laparotomy, inoperable. Premedication, pethidine 50 mg., atropine 1/120 grain (0.5 mg.). Induction with thiopentone 150 mg., nitrous oxide, oxygen, ether; intubation. Maintenance with nitrous oxide, oxygen, ether; relaxation with 0.1 per cent suxamethonium drip. Profound fall in blood pressure to 80/50 mm.Hg after induction and initial intra-abdominal exploration. Ouabain 0.25 mg. at O. Good response; blood pressure rose to 140/90 mm.Hg, but then fell to previous level 20 minutes later, illustrating a limited duration of action of ouabain in this case.

F. *Use of ouabain in circulatory depression associated with cardiac arrhythmia.*

Case VII. F.W. Male, 70.

Appendicectomy for acute appendicitis. Premedication, morphine 1/8 grain (8 mg.) atropine 1/120 grain (0.5 mg.) Induction with cyclopropane, nitrous oxide, and ether; intubation; maintenance with nitrous oxide, ether and d-tubocurarine chloride. After 15 minutes, the heart was irregular (" dropped beats "). Ouabain 0.125 mg. was given, and the pulse became regular within 2 minutes.

Case VIII. M.E.P. Female, 76.

Excision of axillary metastasis nine years after

radical mastectomy. Premedication, morphine 1/6 grain (10 mg.), atropine 1/120 grain (0.5 mg.). Induction with nitrous oxide, chloroform and ether; intubation; maintenance with nitrous oxide and ether (light first plane). There was very little blood loss. Blood pressure began to fall after 15 minutes. At 40 minutes, it was 90/40, pulse rate 80, and irregularly irregular. The veins were distended. No intravenous fluid was given. Ouabain 0.25 mg. was administered at 42 minutes. At 52 minutes, the blood pressure was 125/45, pulse rate 100, but regular, save for occasional extrasystoles.

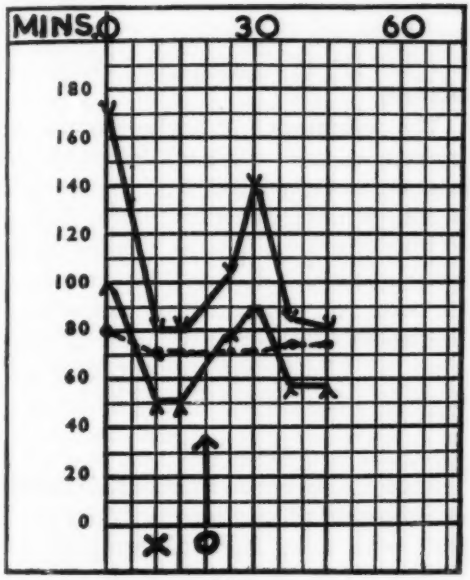

FIG. 6

DISCUSSION

Wiggers (1947), in an article upon the role of myocardial depression in shock, mentioned the possible state of affairs where cardiac reserve mechanisms are already fully in play to compensate for myocardial depression, and where a reduction in venous return (as from blood loss or vasodilatation) or further depression of the heart muscle (from hypoxia or anaesthesia) might rapidly lead to circulatory failure. He suggests the possibility that " cardiac stimulants used in proper dosage and at the proper time might reverse the circulatory failure where transfusions fail ". This suggestion was followed up by Sankey and Crawford (1950), who used intravenous ouabain as an aid to the treatment of traumatic shock. Ouabain had been used experimentally by Kohlstaedt and Page (1944), who had observed that cardiac dilatation after prolonged hypotension was an important sign of impending terminal shock when transfusion alone failed, and by Glasser and Page (1948), who, however, found that ouabain did not affect the survival rate in their animals, though it lessened the harmful effects of over-transfusion. Similarly, the effect of digitalis on the hypodynamic failing myocardium may be lost in the terminal stages of failure (McMichael, 1952).

The usual demonstrable action of digitalis is to strengthen the contraction of the failing ventricle, and full intravenous doses cause a rise in arterial blood pressure, due to a rise in peripheral vascular resistance (McMichael, 1952). Both digitalis and strophanthin preparations have similar properties of myocardial stimulation when dosage is comparable (Walker, Lourie and Burn, 1950).

Ouabain appeared to be the drug of choice for the purpose which we had in mind because its action is rapid. Its effect upon the blood pressure occurs within 3–8 minutes, and may pass off in 15–30 minutes (McMichael, 1950), as we noted clinically. This action may precede the beneficial effects upon the myocardium (McMichael, 1952), so that clinical improvement in the myocardial depression of shock may be expected to remain even if the blood pressure returns to the level present before the administration of the

drug. When the dosage is adequate, the initial blood pressure rise may be maintained in shock as the myocardial stimulant effect takes over after the intitial effect on blood pressure has passed off, and circulatory improvement continues. If the dose is inadequate the initial rise is transient or negligible.

The effect upon blood pressure may not be seen with doses below 0.75 mg. of ouabain (McMichael, 1950). In some of our cases an initial dose of 0.25 mg. produced no response, whereas, when the dose was repeated after 10 minutes, there was a definite rise in blood pressure, suggesting that the initial dose was inadequate. We had chosen the smaller initial dose as our standard, because it was in keeping with the generally accepted therapeutic dose; with further experience, and the conviction of the safety of the drug, we are now prepared to give 0.5 mg. of ouabain initially.

We feel that the use of ouabain, either alone or in conjunction with transfusion, is a valuable aid in the treatment of hypotension occurring during surgical anaesthesia, and in pre- and post-operative resuscitation. We have seen no untoward effects following its use.

When confronted with a case of shock, whether haemorrhagic or otherwise, which fails to respond to intravenous blood-volume replacement, it is now our practice to try the effect of ouabain before proceeding to employ intra-arterial transfusion. In most cases, the response has been so gratifying as to render the more drastic procedure unnecessary, and we feel that this sequence of therapy should always be followed.

SUMMARY

The use of ouabain (intravenously in a dose of 0.25 mg.) in the treatment of shock, with or without replacement of blood-volume, is described in 73 patients (100 administrations). Improvement of the circulatory state followed in 84 per cent; in the remaining cases, failure to respond was associated with continued or renewed trauma or to inadequate dosage of ouabain.

We recommend strongly the use of ouabain in cases of shock in which the response to intravenous fluid replacement is disappointing, whether before, during, or after operation, and as a prophylactic in cases in which deterioration is expected to occur on induction of anaesthesia, movement of the patient, etc.; in those cases in which improvement does not occur, the drug appears to do no harm.

ADDENDUM

Recently, we have administered ouabain on a number of occasions in a dose of 0.5 mg., with even more encouraging responses. This second series is still too small to be worth reporting, but we incline to the belief that the larger dosage will, in future, become routine with us.

REFERENCES

Glasser, O., and Page, I. H. (1948). *Amer. J. Physiol.*, **154**, 297.

Kohlstaedt, K. G., and Page, I. H. (1944). *Surgery*, **16**, 430.

Martindale (1952). *The Extra Pharmacopoeia*. London: The Pharmaceutical Press.

McMichael, J. (1950). *Pharmacology of the Failing Human Heart*. Oxford: Blackwell Scientific Publications.

—— (1952). *Brit. med. J.*, **2**, 525.

Sankey, B. B., and Crawford, T. I. (1950). *Curr. Res. Anesth.*, **29**, 148.

Walker, J. M., Lourie, E. M., and Burn, J. H. (1950). *Brit. J. Pharmacol.*, **5**, 306.

Wiggers, C. J. (1947). *Amer. Heart J.*, **33**, 633.

Brit. J. Anaesth. (1955), **27**, 145.

ANNOTATION

NEUROMUSCULAR TRANSMISSION IN THE NEWBORN

THE advances in medical science during the last half-century are nowhere more dramatically illustrated than in the neonatal mortality figures. The remarkable reductions in the death rate in early life from non-surgical disease has thrown the congenital abnormalities into much sharper relief, and has increased the importance of those conditions as a cause of neonatal death (Rickham, 1952). The range of surgery for the relief of conditions which threaten life in its early days is increasing. In some centres the more serious cases of cyanotic and acyanotic congenital heart disease are being operated on in the first weeks of life, and the interest in abdominal surgery of the newborn is reflected in the volume of literature on the subject.

If anaesthesia in this country is to maintain in this field the high prestige it enjoys in adult surgery, further studies of the peculiarities of neonatal physiology will be necessary. The transition from intra-uterine to extra-uterine life is not accompanied by an equally abrupt change in the physiological pattern of the organism. This is illustrated, for example, by the persistence during early weeks of independent life of the foetal type of haemoglobin compound, the oxygen dissociation curve of which is better adapted to respiratory exchange *via* the placenta than *via* the lungs (McCarthy, 1943), and by the limited flexibility of renal function at birth (McCance, 1948). It has, moreover, been shown recently that the neonate has a distinctive type of response to trauma, which differs in a fundamental way from the adult type of response, and that following surgery there is a much less obvious tendency for the intracellular potassium to become mobilized (Rickham, 1955).

This feature of neonatal physiology is interesting when considered in relation to the findings of Dr. A. L. Stead, published on another page of this issue. Dr. Stead shows that the neonatal infant responds to the relaxant drugs in a way that is qualitatively different from the adult patient. He shows that whereas the sensitivity, weight for weight, of the infant to d-tubocurarine chloride, is high as compared with the adult, the converse is true of suxamethonium. This type of reaction is well known in adult patients with certain abnormalities of the hormonal or endocrine systems. It would appear that Dr. Stead's results are the reflection of another difference between the biochemistry of the infant and the adult. The teleogical significance of this is not as obvious as in the case of some of the other peculiarities of neonatal life, but it may well be that it is related to the necessity for muscular relaxation of the infant during the process of birth.

Cases are reported of d-tubocurarine chloride having been administered to young infants who have subsequently not breathed (Roberts, 1950) and enquiries among those who anaesthetize infants reveal many unpublished cases of delay or failure of recovery from the effect of this drug. It was stated by Rees (1950), before the introduction of the modern brief-acting depolarizing agents, that relaxant drugs should not be administered to the newborn, and it would seem that there was a good reason for adopting this view at that time, when the choice of relaxant drugs was more limited. In the light of Dr. Stead's findings it is necessary to revise such views. It must, however, be recalled that a late "competitive" type of block may follow administration of depolarizing agents. If the order of dosage of suxamethonium used in the infant is high the danger of a persistent myoneural block resulting from this type of action is probably greater than in the adult patient. The clinical use of large doses of this drug in neonates has suggested that this might be the case, and it would seem wise in the present state of knowledge to use, in the neonate, a technique of anaesthesia in which relaxation and immobility over long periods of time are not solely achieved by relaxant drugs.

REFERENCES

McCance, R. A. (1948). *Physiol. Rev.*, **28**, 331.
McCarthy, E. F. (1943). *J. Physiol. (Lond.)*, **102**, 55.
Rees, G. J. (1950). *Brit. med. J.*, **2**, 1419.
Rickham, P. P. (1952). *Lancet*, **1**, 332.
—— (1955). Personal communication (in press).
Roberts, F. W. (1950). *S. Afr. med. J.*, **24**, 167.

Brit. J. Anaesth. (1955), **27**, 146.

A MODIFICATION OF THE CYPRANE HAND-OPERATED RESPIRATORY PUMP

BY

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THE pump described by Eastwood and Harbord (1954), used in conjunction with a spirometer to measure controlled respiratory inflations, has been modified to allow for its operation with nitrous oxide and oxygen without carbon dioxide absorption, the whole of each expiration being removed.

An instrument, see figure 1, has been made so that either method can be employed, the change being regulated by the operation of a lever O, converting the first position (shown diagramatically in figure 2) into the modified position (see figure 3). Its purpose is to draw a consistent tidal volume of gas from a reservoir or suitable patient-demand anaesthetic apparatus, to inflate the patient's lungs, to allow each expiration to pass to a recording spirometer for measurement, and finally to discharge the spirometer to the atmosphere.

FIG. 1
Photograph of respiratory pump

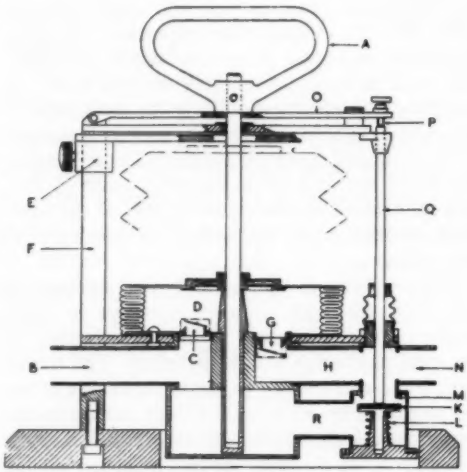


FIG. 2
Diagram of respiratory pump—method 1

When the handle A (continuing with figure 3) of the pump is raised, gas is drawn through the tube B and non-return valve C to the bellows D. The volume which can be drawn from the

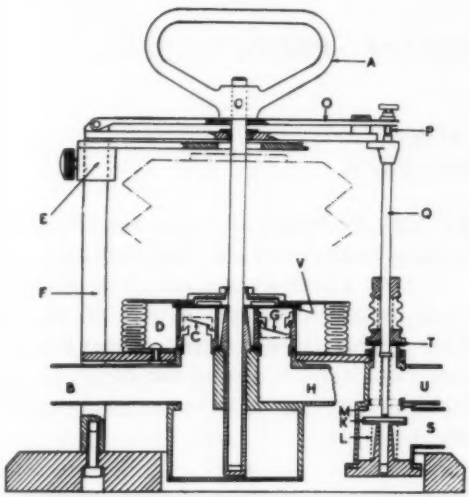


FIG. 3
Diagram of respiratory pump—method 2

reservoir or patient-demand apparatus can be varied and set by adjusting the position of a stop E on the upright guide F.

On the downstroke the valve C closes, shutting off the reservoir or patient-demand apparatus, and the valve G opens, allowing gas to pass into the tube H, which is connected to the patient by a corrugated tube.

The patient is also connected to the tube S by a second corrugated tube; both tubes being connected by a large bore Y-piece, into which fits the metal endotracheal mount. The tube U is connected to a spirometer.

During the greater part of the downstroke the valve K is held closed on its seat M by a spring L. The gases from the bellows D therefore pass into the patient's lungs. When the end of the downstroke is almost reached, the handle A touches a lever O, carrying an adjustable screw P, which presses on the movable rod Q.

Depression of the rod Q first causes the valve T to close, shutting off all connection between the spirometer and the atmosphere. Slight further depression opens the valve K, allowing the patient's exhalation to pass into the spirometer for measurement. At the same time the rubber seat V shuts off all connection between the reservoir or patient-demand apparatus and the patient and spirometer system.

On raising the handle A to recharge the bellows for the next inspiration, first the valve K closes and the rubber seat V opens. Next the valve T opens and allows the spirometer to discharge its contents into the atmosphere and so the cycle is repeated.

It is necessary to weight the spirometer bellows slightly to ensure that it deflates rapidly enough before the following expiration begins. The patient should be completely apnoeic before this pump is put into operation; if the return of spontaneous respiration is suspected it will be shown by the movements of the spirometer when the handle A is kept fully depressed for a short period.

The respiratory tracing shows the same characteristics for both positions of the pump (Eastwood and Harbord, 1954); an upstroke represents emptying of the spirometer, the horizontal interval the period of inflation, and the downstroke represents the filling process as gases pass from the patient into the spirometer.

ACKNOWLEDGMENTS

My thanks are due to Messrs. Cyprane Ltd., Keighley, Yorkshire, who modified the apparatus.

REFERENCE

Eastwood, A. B., and Harbord, R. P. (1954). *Brit. J. Anaesth.*, **26**, 197.

Brit. J. Anaesth. (1955), **27**. 148.

A MODIFIED LARYNGEAL SPRAY

BY

P. L. F. MORTIMER

Frenchay Hospital, Bristol

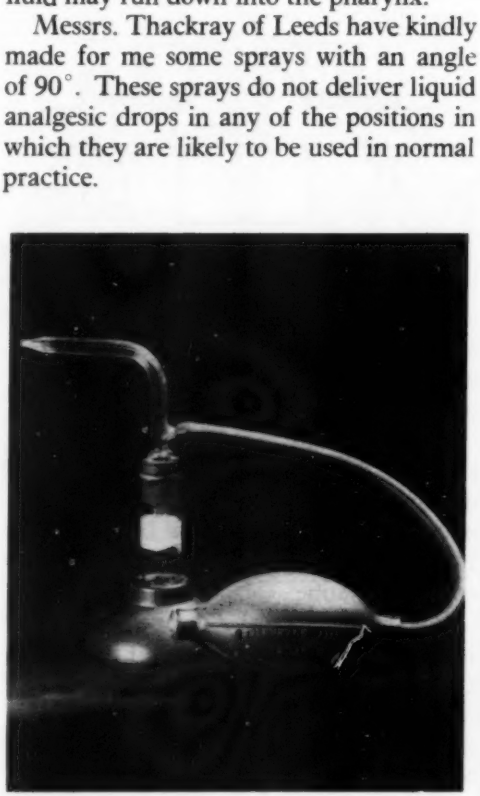
THERE is a large number of different laryngeal sprays available, and the excuse for adding to this list is that the sprays I am now using are more satisfactory than others I have tried.

Nebulizers which are complicated in design, and contain metal capillary tubes, suffer from the defect that unless they are washed clean after each occasional use—a costly matter, and troublesome—they soon become attacked by the alkaloid used as analgesic. Crystals deposit, and when the spray is taken off the shelf for use in a hurry it either blows nothing but air or delivers large and dangerous drops into the pharynx.

The Rogers all-glass spray does not react in any way with the analgesic solution. It can be placed on the shelf after use and taken down again weeks later, and will immediately deliver a fine spray with no large drops. This spray, moreover, extends for about a yard from the nozzle, and can easily be operated with one hand. There is therefore no need to thrust any part of the spray into the pharynx, a procedure which is all too often the cause of movement of the laryngoscope and the elicitation of unsuppressed pharyngeal reflexes.

The angle of the nozzle on the stem of the Rogers spray is about 120°. It is possible that when it is used with the patient supine, with the laryngoscope in position for direct spraying of the cords, the reservoir may be higher than the nozzle, and fluid may run down into the pharynx.

Messrs. Thackray of Leeds have kindly made for me some sprays with an angle of 90°. These sprays do not deliver liquid analgesic drops in any of the positions in which they are likely to be used in normal practice.



I have used Rogers sprays for many years with 10 per cent cocaine/hydrochloride solution, and have never produced yet any symptom or sign of overdose or "idiosyncrasy". Perhaps I have been lucky.

Brit. J. Anaesth. (1955), **27**, 149.

MODIFICATION OF MACINTOSH'S LARYNGEAL SPRAY

BY

ALEX C. FORRESTER

Glasgow Royal Infirmary

THIS spray was designed to be used in conjunction with a Macintosh's laryngoscope (fig. 1).

The limb carrying the jet of the conventional Macintosh spray has been made rigid and shaped to the curve of a Macintosh blade. It is of sufficient length to pass easily between the cords, and allows of accurate placing of the analgesic agent in and around the larynx. It can be used comfortably with one hand allowing the other free to manipulate the laryngoscope. It may be sterilized by inserting the metal limb in boiling water.

It is obtainable from Messrs. A. Charles King Ltd., London, W.1.

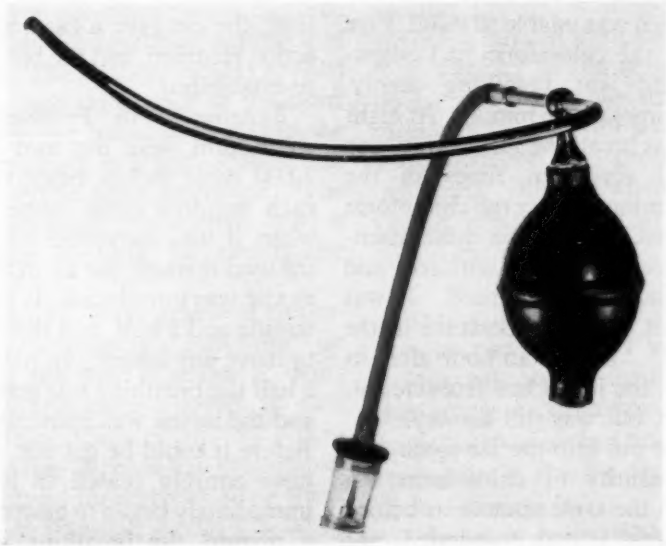


FIG. 1

Forrester–Macintosh Spray

ON CHLOROFORM AND OTHER ANÆSTHETICS

THEIR ACTION AND ADMINISTRATION

BY

JOHN SNOW, M.D.

Licentiate of the Royal College of Physicians

(*Continued from page* 110)

Experiment 15. A cat was put into the jar holding 3,000 cubic inches, and 82.5 grains of chloroform were introduced, being two grains and three-quarters to each hundred cubic inches (2.2%). In five minutes, it had evaporated, and the cat began to stagger in its walk. In two minutes more, it was unable to stand. Five minutes after the chloroform had evaporated, the cat was breathing deeply, seventy-five times in the minute. At eight minutes, it was breathing less deeply, one hundred and seventeen times in the minute. Ten minutes after the chloroform had evaporated, the cat was quite insensible, and breathing one hundred and twenty-six times in the minute. It was now taken out. The temperature in the axilla was 98°. In half an hour after its removal from the jar, it had recovered its consciousness, but was still drowsy.

It was now put into the jar again, and the same quantity of chloroform was introduced in the same manner as before. In five minutes, it had evaporated, and the cat was again insensible. In other five minutes, it was breathing rather deeply, forty-eight times in the minute. Twelve minutes after the chloroform had evaporated, the cat was breathing in the same manner, but sixty-eight times in the minute. The breathing afterwards became shallow and feeble, and half an hour after the chloroform had evaporated, it was eighty-eight in the minute. In five minutes more, the breathing ceased. The cat was taken out of the jar, and the stethoscope was applied to the chest. The heart could not be heard to beat at first, but in a short time, the cat gave a gasp, and the heart's action returned, and the breathing became re-established.

Experiment 16. Forty-eight grains of chloroform were put into a jar holding 1,600 cubic inches, being three grains to each hundred cubic inches (2.4%), and when it was converted into vapour and diffused through the air in the jar, a white mouse was introduced. It ran about for a minute and a half, and then it was unable to move any longer. In nine minutes and a half the breathing was getting very slow, and the mouse was immediately removed. Before it could be got out, it appeared to have entirely ceased to breathe, but it immediately began to gasp at intervals. In a minute, the breathing improved, and soon became natural. Three minutes after its removal, the mouse began to walk in a ring, and in seven minutes, it had quite recovered.

Experiment 17. A guineapig was placed in a jar holding 1,600 cubic inches, and fifty-four grains of chloroform were intro-

duced on blotting paper, in the manner previously explained; being three grains and three-eighths to each hundred cubic inches of air (2.7%). In four minutes, the chloroform had evaporated, and become diffused through the air in the jar and the guinea-pig was drowsy. In three minutes more, it was lying apparently insensible, and breathing feebly, thirty times in the minute. After this, it kicked occasionally for a few minutes. When six minutes had elapsed from the time when the chloroform had evaporated, the breathing was very feeble, and apparently performed only by the diaphragm. From fifteen to eighteen minutes, I could hardly see whether the animal was breathing or not, and it was taken out of the glass at eighteen minutes, when the breathing appeared to have ceased. The stethoscope was applied to the chest, and the sounds of the heart could scarcely be heard at first, but the breathing returned in a few seconds, and the action of the heart improved. The guineapig gradually recovered, but it was not able to walk for twenty-five minutes.

Experiment 18. Sixty grains of chloroform were introduced into the jar employed in the last experiment, being three grains and three-quarters to each hundred cubic inches of air (3%) contained in the jar. When it had evaporated, and was diffused through the air, a white mouse was introduced, whilst the lid of the jar was moved a little to one side for a moment. It ran about at first, but suddenly ceased to run, and became insensible, at the end of three-quarters of a minute. It lay breathing deeply and rapidly till two minutes had elapsed, when the respiration became slow, and it ceased at two minutes and three-quarters after the mouse was introduced. It was removed at this time, and it gasped a few seconds afterwards; this gasp was soon followed by another; the gaspings became more frequent, and in a short time, the natural breathing was resumed. In five minutes, the mouse was able to walk.

The third, fourth, and fifth of the above experiments show that one grain of chloroform to each hundred cubic inches (0.8%) of air suffices to induce the second degree of narcotism, or that state in which consciousness and voluntary motion are disturbed, but not entirely abolished. Now one grain of chloroform produces 0.767 of a cubic inch of vapour at 60°, when its specific gravity is 4.2; and, when the vapour is inhaled it expands somewhat, as it is warmed to the temperature of the lungs; but it expands only to the same extent as the air with which it is mixed, and therefore the proportions remain unaltered. But air, when saturated with vapour of chloroform at 100°, contains 43.3 cubic inches in 100; and

as 0.767 : 43.3 : : 0.0177 : 1.

So that if the point of complete saturation be considered as unity, 0.0177 or 1-56th, will express the degree of saturation of the air from which the vapour is immediately absorbed into the blood; and, consequently, also the degree of saturation of the blood itself.

I find that serum of blood at 100°, and at the ordinary pressure of the atmosphere, will dissolve about its own volume of vapour of chloroform; and since chloroform of specific gravity 1.483 is 288 times as heavy as its own vapour, 0.0177 ÷ 288 gives 0.0000614, or one

part in 16,285, as the average proportion of chloroform by measure in the blood, in the second degree of narcotism.

It is evident, from the experiments numbered 9 to 12 inclusive, that two grains of chloroform to each hundred cubic inches (1.6%) of the inspired air cause a state of very complete insensibility, corresponding with what I have designated the fourth degree of narcotism; and by the method of calculation employed above we get 0.0354, or 1-28th, as representing the degree of saturation of the blood, and 0.0001228 the proportion by measure in the blood.

In experiments 6, 7, and 8, in which quantities of chloroform were employed intermediate between one and two grains to each hundred cubic inches of air a moderate amount of insensibility was induced, corresponding very much with the state of patients during operations under chloroform.

The experiments from 13 to 18 show that quantities of chloroform, exceeding two grains to 100 cubic inches of air (1.6%), have a tendency to embarrass and arrest the function of respiration, if the inhalation is continued. I have not yet been able to determine satisfactorily the exact proportion of chloroform which requires to be absorbed to arrest the respiration of animals of warm blood. I believe there is a definite proportion which has this effect, but there are two reasons why it is not so easy to ascertain it, as to ascertain the proportion which causes the minor degrees of narcotism. In the first place, the breathing often becomes very feeble before it ceases, so that the animal inhales and absorbs but very little chloroform, and remains on the brink of dying for some time. In the next place, the temperature of the body falls in a deep state of narcotism, especially in small animals; and, as the temperature falls, the amount of chloroform which the blood can dissolve from any given mixture of air and vapour increases.

Judging from the experiments numbered 14 to 18, three grains of chloroform to each hundred cubic inches of air (2.4%) must be very nearly the quantity which has the power of arresting the breathing when the temperature of the body is 100°; and as three grains of chloroform produce 2.3 cubic inches of vapour, and air at 100° is capable of taking up 43.3 per cent. of its volume, it follows that the blood must contain between 1-18th and 1-19th as much chloroform as it is capable of dissolving, at the time when the respiration is arrested. In the 14th experiment, the breathing of the two mice was on the point of being stopped by two and a half grains of chloroform in each hundred cubic inches of air (2%), but during the thirteen minutes which the mice breathed the vapour, their temperature fell to about 90°. Air, when saturated with the vapour of chloroform at this temperature, contains 35 per cent., and two grains and a half of chloroform yield 1.917 cubic inches of vapour: so by a calculation similar to that made at page 151, the mice at the time when the breathing was about to cease must have absorbed 1-18th part as much chloroform as their circulating fluids were capable of dissolving.

The reader will have observed that, in the experiments related above, the mice became much more quickly affected than the guineapigs and cats. The reason of this is their quicker respiration and

circulation, and much more diminutive size. Little birds, such as linnets and sparrows, are also very quickly affected by chloroform. Frogs are more slowly affected, owing to their languid respiration, unless the vapour to which they are exposed is very strong.

They can, however, owing to their low temperature, be rendered insensible by proportions of vapour too small to affect animals of warm blood; and as they have no proper temperature of their own, the amount of vapour (in proportion to the air in which they are placed) that will affect them, depends entirely on the temperature of that air.

The following experiment was several times performed on frogs with the same result, the temperature of the room being about 55°, as it was in winter.

Experiment 19. 4.6 grains of chloroform were diffused through the air of a jar of the capacity of 920 cubic inches (0.4%), and a frog was introduced. In a few minutes, it became affected, and at the end of ten minutes, was quite motionless and flaccid; but the respiration was still going on. Being now taken out, it was found to be insensible to pricking: it recovered in a quarter of an hour.

In a repetition of this experiment, in which the frog continued a few minutes longer in the vapour, the respiration ceased, and the recovery was more tardy. On one occasion, the frog was left in the jar for an hour, but when taken out, and turned on its back, the pulsations of the heart could be seen. In an hour after its removal, it was found to be completely recovered.

The first of the experiments related above (page 107), showed that an atmosphere containing half a grain of chloroform to each hundred cubic inches, produced scarcely any appreciable effect on animals of warm blood; but the following calculation explains why this quantity acts so energetically on the frog, and proves that this creature is affected by chloroform according to the same law as animals of warm blood. The vapour is absorbed into the blood and lymph of the frog at the temperature of the external air, whose point of relative saturation therefore remains unaltered, both in the lungs and in contact with the skin of the animal; and as half a grain of chloroform produces 0.383 cubic inches of vapour, and air at 55° contains, when saturated, 10 per cent. of vapour 0.0383, or 1-26th, expresses the degree of saturation of the air, and also of the blood of the frog. And this is a very little more than the quantity (0.0354 or 1-28th) which was calculated above to be the greatest amount which could be absorbed with safety into the blood of mammalia. It must be observed, however, that the pulmonary respiration of the frog was arrested by this proportion of 1-26th as much chloroform as the blood would dissolve, whilst we calculated that it required about as much as 1-18th to arrest the breathing of animals of warm blood. It must be remembered, however, that the pulmonary respiration of frogs is a process of swallowing air, which only goes on when the creature is comparatively active. In the torpid state, the respiration takes place only by the skin, and the frog never breathes with the aid of the same muscles and nerves as mammalia and birds.

By warming a frog, together with the air in which it is placed, it is, in accordance with the law explained above,

rendered comparatively proof against an amount of chloroform which would otherwise render it insensible.

Experiment 20. A frog, which had been a few days previously subjected to the experiment just narrated, was put into the same jar, which was placed near the fire, till a thermometer inside marked 75° Fah.; 4.6 grains of chloroform (0.4%) were then introduced and diffused through the air in the jar. The jar was kept for twenty minutes, with the thermometer indicating the same temperature within one degree. For the first seventeen minutes, the frog was unaffected; and only was dull and sluggish, but not insensible, when taken out. Air at 75°, when saturated with vapour of chloroform, contains 22 per cent., and therefore the 0.383 per cent. of vapour, which at 75° was capable of saturating the fluids of the frog to the extent of 1-26th of what they would dissolve, was, at 75°, capable of saturating them only to the extent of 1-57th.

At one of Dr. Wilson's Lumleian Lectures, at the College of Physicians, on March 29th, 1848, I had the honour of performing some experiments, and making some remarks, on chloroform, and I combined together two experiments on frogs and small birds, in a way which shows how entirely the effects of a narcotic vapour depend on the quantity of air with which it is mixed, and on other physical conditions.

Experiment 21. I introduced a chaffinch, in a very small cage, into a glass jar holding nearly 1,000 cubic inches, and put a frog into the same jar, covered it with a plate of glass, and dropped five grains of chloroform (0.4%) on a piece of blotting paper suspended within. In less than ten minutes, the frog was insensible, but the bird was not affected.

Experiment 22. I then placed another frog and another small bird in a jar containing but 200 cubic inches, with exactly the same quantity of chloroform (2%). In about a minute and a half, they were both taken out,—the bird totally insensible, but the frog not appreciably affected, as from its less active respiration it had not had time to absorb much of the vapour.

The blood in the human adult is estimated by M. Valentin to average about thirty pounds. M. Valentin's experiments were so conducted that this quantity must include the extra vascular liquor sanguinis, as well as the blood actually contained within the vessels. On this account, his estimate is all the better fitted for calculating the amount of chloroform absorbed, since this medicine, when inhaled gradually, passes by exosmosis through the coats of the blood-vessels into the fluid in which the tissues are immediately bathed. The above quantity of blood would contain 26 pounds 5 ounces of serum, which, allowing for its specific gravity, would measure 410 fluid ounces. This being reduced to minims, and multiplied by 0.0000614, the proportion of chloroform in the blood required to produce narcotism to the second degree (see page 151), gives 12 minims as the whole quantity of the blood. More than this is used in practice, because a considerable portion is not absorbed, being thrown out again when it has proceeded no further than the trachea, the mouth and nostrils, or even the face-piece. But I find that if I put twelve minims into a bladder containing a little air, and breathe it over and

over again, in the manner of taking nitrous oxide, it suffices to remove consciousness, producing the second degree of its effects.

To induce the third degree of narcotism, or the condition in which surgical operations are usually commenced, would require that about 18 minims should be absorbed by an adult of average size and health, according to the above method of calculation; and to induce the deep state of insensibility, which I have termed the fourth degree of narcotism, would require 24 minims; whilst to arrest the function of respiration would require that about 36 minims should be absorbed.

PREPARATIONS FOR INHALING CHLOROFORM

The only direction which it is usually requisite to give beforehand, to the patient who is to inhale chloroform, is to avoid taking a meal previous to the inhalation; for chloroform is very apt to cause vomiting, if inhaled whilst there is a quantity of food in the stomach. The sickness is not attended with any danger, but it constitutes an unpleasantness and inconvenience which it is desirable to avoid. The best time of all for an operation under chloroform is before breakfast, but the customs and arrangements of this country do not often admit of that time being chosen, and it is unadvisable to make the patient fast beyond his usual hour. It answers very well to perform an operation about the time when the patient would be ready for another meal, or, if the time of operation fall two or three hours after the usual time of eating, to request the patient to make only a slender repast at that time, so as just to prevent the feeling of hunger. It is impossible to prevent vomiting in some cases with the best precautions, for the stomach occasionally will not digest when the patient is expecting a surgical operation, and the breakfast may be rejected in an unaltered state hours after it has been taken. In other cases the patient does not vomit, even when he inhales chloroform shortly after a full meal.

(*To be continued*)

WORLD CONGRESS OF ANESTHESIOLOGISTS, SCHEVENINGEN

In some categories of hotel accommodation the available allotment of beds is almost exhausted. The Organizing Committee has still a limited number of beds at its disposal, and would have until March 31, but not later. Those wishing to attend are recommended to send urgently their explicit order for rooms to the following address:

WORLD CONGRESS OF ANESTHESIOLOGISTS, BILTHOVEN, HOLLAND.

(Informative data furnished on the yellow application forms are not to be considered as definite hotel orders.)

CORRESPONDENCE

REBREATHING WITH A SEMI-CLOSED CIRCUIT

Sir,—I would like to comment briefly on Dr. Bullough's letter (1955) about the article on "Rebreathing with a Semi-closed System" by Lind and myself (1954). Dr. Bullough asserts that our conclusions are invalidated by the substitution of a water valve for a spring-loaded one, baldly stating that the two behave quite differently. The only practical difference in their behaviour is that a water valve regularly blows off at the same tension: a spring-loaded one does not; and we made the substitution in order to eliminate an uncontrollable variable. As our results show, carbon dioxide accumulation was not, in fact, affected by wide variations of this tension, so that we cannot admit the justice of Dr. Bullough's claim.

Though it is true that in human subjects breathing into semi-closed systems the concentration of CO_2 in the inspired mixture may be affected by changes in the pattern of respiration, our experiments were designed to hold this pattern constant. The duration of inspiration, expiration and pause, though not explicitly stated, can be deduced from our paper. The piston of the respiratory pump was worked by reciprocating motion from a motor-driven crankshaft. There was therefore no respiratory pause, and both phases of respiration were equal. They lasted (at 16 respirations a minute) for 1.9 seconds. This form of respiration is, of course, similar to that which occurs during anaesthesia. CO_2 was liberated into the anaesthetic system under study throughout each expiratory phase at a rate chosen to conform to the expected metabolism of an anaesthetized patient. Conditions occurring clinically were thus, we believe, closely simulated, but with the important difference that they were known to be constant throughout each experiment.

Variations in metabolism, in the form and depth of respiration, and in transport of CO_2 cannot be eliminated entirely from experiments made with human subjects, and these variations no doubt contribute to the differences, mentioned by Dr. Bullough, to be found in published results. We hold that it is only by the rigid elimination of uncontrollable variables that progress can be made in the study of this problem, and that is why we think that—in spite of Dr. Bullough's doubts—our work may have some clinical significance.

RONALD WOOLMER
University of Bristol

REFERENCES

Bullough, J. (1955). *Brit. J. Anaesth.*, **27**, 47.
Woolmer, R., and Lind, B. (1954). *Brit. J. Anaesth.*, **26**, 316.

OUR annotator writes:

Part of Dr. Bullough's letter (1955) condemns in strong terms the section of the annotation on "Rebreathing in Anaesthetic Circuits" which deals with papers by Mapleson and by Woolmer and Lind in the same issue (1954). It may be advisable to assist the reader in deciding for himself if Dr. Bullough's apparently powerful arguments possibly "rest on a defective foundation, to put it mildly".

Dr. Bullough claims that any conclusions based on the approximate relation, average inspiratory flowrate (AIF) equals twice the respiratory minute volume (RMV), are "*invalid*". According to him the relation should be AIF = 5 (or 6) × RMV, and a paper by Orkin *et al.* (1954) is quoted in evidence as a secondary reference.

Orkin *et al.* are concerned with the resistance of endotracheal equipment but mention in somewhat vague terms a relation between a "normal flowrate" and the RMV (ibid., p. 220). The original investigations quoted by Orkin in this connection are those by Mead (1953), Cherniack (1952), and Proctor (1950). Even a short study of these original papers will convince the unbiased reader that none of the authors makes the extraordinary statement (AIF = 5 × RMV) attributed to them by Dr. Bullough. In actual fact, the quantity discussed by them repeatedly is the *maximum* (or peak) of the *instantaneous* inspiratory flowrate *v.* time-curve. On the other hand, this maximum flowrate does not enter at all into the

theory of the investigations mentioned in the annotations; the main quantity is always the *average* inspiratory flowrate (or V_t/T_1 in Mapleson's terminology). The annotation stated clearly the basis for the approximation: $AIF = 2 \times RMV$; there is experimental evidence that the numerical factor is nearer 2.2 in normal unimpeded respiration (Proctor, 1949, table III), but this point is not under discussion.

The remainder of Dr. Bullough's criticisms seem to be of a less serious nature:

The annotator took an arbitrary maximum of 0.2 per cent CO_2 in the inspired air as reference level in order to compare the various theories and experiments under discussion. The choice of this level may be made plausible by stating that (*a*) Woolmer and Lind mention 0.2 per cent CO_2 as a satisfactory level (ibid., p. 321); (*b*) many breakthrough tests of sodalime canisters are concluded at levels of 0.2 to 0.5 per cent escaping into the circuit, e.g. Robson and Pask (1954; fig. 2) and Adriani (1941; fig. 2A). It is not easy to follow Dr. Bullough's argument that the choice of an 0.2 per cent CO_2 level is "unrealistic" because subjects breathing from a semi-closed system in experiments by Swartz (1953) were "unable to prevent a concentration of 0.9 per cent CO_2 in the inspired mixture". As one of the subjects had a RMV = 8.6 l. and the fresh gas flow was only F = 8 l./min, the high CO_2 level would not appear surprising in the light of the work by Molyneux and Pask.

Dr. Bullough further complains of the expression "Ayre's T-piece" used in the annotation to describe the structure illustrated in figure 3 of the paper by Woolmer and Lind, but does not mention that a qualifying term "with large tube" was added to differentiate it from the original device. However, a case can be made against linking the name of an original device with any subsequent modifications, although this practice seems to be quite common (e.g., Woolmer and Lind, 1954, p. 318; Kelsall, 1954).

REFERENCES

Adriani, J., and Byrd, M. L. (1941). *Anesthesiology*, **2**, 450.
Bullough, J. (1955). *Brit. J. Anaesth.*, **27**, 47.
Cherniack, R. M., *et al.* (1952). *J. Clin. Invest.*, **31**, 1028.
Kelsall, P. D. (1954). *Brit. J. Anaesth.*, **26**, 445.
Mead, J., and Wittenberger, J. L. (1953). *J. Applied Physiol.*, **5**, 779.
Orkin, L. R., *et al.* (1954). *Cur. Res. Anaesth.*, **33**, 217.
Proctor, D. F., and Hardy, J. B. (1949). *Bull. Johns Hopkins Hosp.*, **85**, 253.
—— *et al.* (1950). *Bull. Johns Hopkins Hosp.*, **87**, 255.
Robson, J. G., and Pask, E. A. (1954). *Brit. J. Anaesth.*, **26**, 333.
Swartz, C. H., Adriani, J., and Mih, A. (1953). *Anesthesiology*, **14**, 437.
Woolmer, R. W., and Lind, B. (1954). *Brit. J. Anaesth.*, **26**, 316.

FACULTY NEWS

ANNUAL GENERAL MEETING AND CLOVER LECTURE

THE Annual General Meeting of the Faculty of Anaesthetists will take place in the Royal College of Surgeons on Wednesday, March 23, 1955, at 4.0 p.m. This is to be followed at 5.0 p.m. by the Joseph Clover Lecture to be given by Professor W. W. Mushin. The title of his lecture is "Measurement in Anaesthesia".

The Seventh Anniversary Dinner of the Faculty, at which all Fellows and Members are entitled to attend will be at 7.15 p.m. on the evening of the Annual General Meeting.

LECTURE COURSES

THE following courses of Lectures of interest to Anaesthetists will be given in the Spring.

On Anaesthesia: March 14—April 1, 1955.

On Pharmacology: May 9—May 20, 1955.

Details and application forms for these courses can be obtained from the Secretary of the Royal College of Surgeons.

ARGENTINE ASSOCIATION OF ANAESTHESIOLOGISTS

WE have received information that the following officers have been elected for the year 1955.

President: Dr. Julio F. Parada.

Secretary: Dra. Margot B. de Oleaga ALarcon.

Treasurer: Dr. Alberto Gonzalez Varela.

SOCIETY OF ANAESTHETISTS OF THE SOUTH-WESTERN REGION

At a meeting of the Society of Anaesthetists of the South-Western Region at Bristol on November 26 and 27, 1954, papers were read by: Dr. A. I. Parry Brown, M.D., F.F.A.R.C.S., Consultant Anaesthetist to the London Hospital; Dr. Michael Johnstone, M.D., F.F.A.R.C.S., Consultant Anaesthetist to the Manchester Royal Infirmary; J. Angell James, Esq., M.D., M.R.C.P., F.R.C.S., Consultant Ear, Nose and Throat Surgeon to the United Bristol Hospitals; Dr. J. H. Challenger, M.B., Ch.B., F.F.A.R.C.S., Consultant Anaesthetist to the United Bristol Hospitals; Dr. R. C. Tudway, M.B., B.S., B.Sc., F.F.R., Radiotherapist-in-Charge, the United Bristol Hospitals.

ANAESTHESIA FOR SOME SIMPLE E.N.T. PROCEDURES

by Dr. Parry Brown

Dealing first with anaesthesia for tonsillectomy and removal of adenoids in children, he described two different techniques. In the first—the guillotine method under single dose ethyl chloride—surgeon and anaesthetist had to take turns for possession of the field. The child was given no sedative premedication, and therefore correct psychological handling was important. The technique required artistry and teamwork; but it allowed large numbers of patients to be treated, it used the minimum of anaesthetic, and return of consciousness was rapid. However, the number of patients who came back for the removal of tonsil remnants, or for the treatment of sequelae such as adhesions, was as high as 10 per cent, which was not good enough.

The second technique he described was therefore preferable because it permitted unhurried surgery. If enough time were taken, during the operation, to secure all vessels which might bleed, premedication was permissible. Ninety minutes before operation the children were given pentobarbital ½ grain per stone. Thirty minutes before operation they were given atropine by injection, and "nepenthe", 1 minim per year, by mouth.

Anaesthesia was induced by large flows of N_2O and O_2 with added CO_2. Ether was brought in as soon as possible, and increased until the gas was bubbling through it in both vaporizing bottles. The ether concentration was reduced, and the gas flow halved, when the operation was begun, and during the first part of it the anaesthetic was delivered through a mouth hook. *The adenoids were curretted first.* This was to allow control of bleeding from this part of the operation to be achieved in the proper way—namely, by pressure—while the tonsillectomy was proceeding. When the adenoids had been curretted, intubation was performed. The tube, which had first been snugly packed with vaselined gauze, was introduced into the nose. The end was picked up in the nasopharynx and brought out of the mouth, and the gauze packing (which had prevented blood from passing into it during its passage through the nose) was removed. The tube was then directed towards the glottis, the larynx was threaded on to it, and the anaesthetic was continued by this route. The tonsils were dissected out and the tonsillar and adenoid fossae carefully inspected for bleeding; then the tube was removed. An adenoid pack and a pharyngeal airway were inserted and secured in position by tapes.

The third anaesthetic technique described was one for submucous resection of the nasal septum. The most important requirement for this was an avascular field. The patients were premedicated with relatively large doses of "Omnopon" and scopolamine. Topical analgesia was then produced by a shortened version of Moffat's instillation technique. The solution used was: 10 per cent cocaine, 2.4 ml.; 1 per cent sodium bicarbonate, 2.4 ml.; 1 in 10,000 adrenalin, 1.2 ml. Sleep was induced with thiopentone; a greased pharyngeal airway was inserted, and the patient was placed in position on the table. It was an important part of the technique to see that nothing got on to the larynx, so the patient was placed supine with the head a little back, and a strip of gauze was placed in each posterior naris. After the resection, each side of the nose was

plugged with a finger of oiled silk stuffed with gauze.

The description of the first technique was illustrated by a film; that of the other two by lantern slides.

THE PHYSIOLOGY OF THE UPPER RESPIRATORY TRACT

by Mr. Angell James

He gave a vivid description of the anatomy and physiology of the nose, pharynx and larynx, and pointed out some contrasts between animals and man. The action of the nasal mucous membrane was to warm the inspired air, to filter it from dust and bacteria and to moisten it. Prominence was given to the role of the cilia, and their movement was beautifully illustrated in a film made by Mr. Negus. To do their work properly, cilia needed the right conditions. Their action was paralysed by drying, and impaired by heat and cold and by some drugs. An intact sheet of ciliated mucous membrane formed an effective barrier to bacteria, but not to viruses. The application of 10 per cent cocaine stopped cilia from working in three minutes. Weaker solutions were less harmful. Adrenalin, applied in solution stronger than 1 in 100,000, slowed them considerably. Ether and chloroform vapour and nitrous oxide had no effect on cilia, but a drop of liquid ether or chloroform killed them at once. The cooling and drying of mucous membranes by the gas stream in insufflation techniques was bad for the cilia on it.

The speaker next referred to reflex responses in the respiratory tract. Stimulation of the asthmagenic zone in the nose led to reflex bronchoconstriction. Radiant heat to the body led to reflex vasodilatation in the nasal mucous membrane with partial nasal obstruction. The nose was sensitive to temperature changes, and chilling of the body led to a lowering of the temperature of the nose, which in turn reduced its resistance to infection.

A second film was then shown. This gave a striking demonstration of ciliary action in man, and of the movements of the palate during coughing, swallowing and phonation. The star was a patient who had had lateral rhinotomy performed, and in whom the interior of one side of the nose was plainly visible. Pus was seen emerging from the frontal sinus and being steadily wafted across the nasal cavity by the action of the cilia.

During the subsequent discussion the speaker said that plastic endotracheal tubes were to be preferred to rubber ones, since plastic material was more inert and less porous than rubber; and it would be an advantage if cuffed plastic tubes were available. Spraying the mucous membrane with cocaine did no lasting damage to the cilia. If adrenaline were used with cocaine the question of absorption was unimportant, and a 10 per cent solution of cocaine had no advantage over one of 5 per cent.

SOME ASPECTS OF THE TREATMENT OF INTRACTABLE PAIN

by Dr. J. H. Challenger

Dealing first with the arrangements for a practical organization to help patients with intractable pain, he said that the main desiderata were understanding and sympathy with the patients, familiarity with a wide range of nerve-blocking techniques, and adequate publicity. When confronted with the patient the anaesthetist had to make an assessment based upon the taking of a good history and a careful physical examination. Not only should the diagnosis and the expected time of survival be considered, but also the patient's mental state. Patients with intractable pain were often emotionally unstable, and their pain threshold was low. The next step was to decide on the plan of action, and an important preliminary to this was to determine the pathways involved in the transmission of the pain. Somatic or autonomic channels might be involved, and in some cases both a somatic and an autonomic block was required.

Procaine was a useful agent for diagnostic and prognostic blocks. For longer blocks 6 per cent phenol might be used. The speaker had not had much success with Efocaine. Intrathecal alcohol was probably the best, and in suitable cases would provide relief of pain for weeks or months.

The results of nerve blocks were difficult to predict, and often disappointing. In the speaker's series of 44 patients, 9, or 19 per cent, had complete and lasting relief; 51 per cent had some relief; and 34 per cent no relief. In half of the patients the pain was confined to the lower part of the back, the pelvis and the legs, and many of them were suitable for intrathecal alcohol; but the risk of paresis of bladder and rectum precluded

its use when the pain was high, and the alternative methods which had to be used in these cases were less successful.

THE ROLE OF THE CARDIOGRAM IN ANAESTHESIA

by Dr. Michael Johnstone

This paper was illustrated with a large number of slides of electrocardiograms. He said that the E.C.G. provided the anaesthetist with information which could be obtained in no other way. Blood pressure measurements did not provide an index of the state of the myocardium; but, since the Purkinje network had the same blood supply as the cardiac muscle fibres, its efficiency, which was reflected in the E.C.G., paralleled that of the cardiac muscle.

Vagal stimulation inhibited the S.A. node and shifted the pacemaker to the A.V. node. Retrograde stimuli travelling from the A.V. node towards the auricle then gave a tracing with the P wave inverted and late. The P wave might come before or after the Q.R.S. complex, or be buried in it. Examples of these three conditions were shown.

When sympathetic tone was increased, other types of disturbance, such as ectopic ventricular beats, were encountered. These might be unifocal, bifocal or multiple, and each type gave a different electrocardiographic pattern. Ectopic ventricular beats could be caused directly by tactile stimulation of the heart, or reflexly by irritation of the larynx. Irritant vapours reaching the vagal receptors in the alveoli in high concentration could result in complete vagal inhibition; but respiration might continue for a time after ventricular standstill from this cause, and the harmful stimulus might in this way be diminished. Reflex vagal inhibition was made more likely by high or total spinal analgesia, but the heart could always be released from vagal inhibition by intravenous atropine.

Sympathetic overactivity was predisposed to by many drugs, such as morphine, trichlorethylene, ethyl chloride and cyclopropane, but gave rise to arrhythmias only if CO_2 retention co-existed. These arrhythmias could be abolished by efficient ventilation, or by activation of the pulmo-cardiac reflex by ether.

In conclusion, he said that there were four ways in which the E.C.G. could be of value to the anaesthetist. Firstly, as an aid in the treatment of severe cardiac collapse during anaesthesia: secondly, in assessing the effect of new drugs on the heart: thirdly, in assessing the condition of a patient considered for, or undergoing, hypotensive anaesthesia, and in following the heart's action when the pulse was impalpable because of hypotension: fourthly, as a monitor of the conduction of the myocardium during operation in any bad risk.

BOOK REVIEW

The Practice of Local Anaesthesia (4th edition). By George Bankoff, M.D., D.Ch., F.R.F.P.S., F.R.C.S.E. Published by Isaac Pitman & Sons Ltd., London, 1954. Pp. 275; 201 illustrations. Price 25*s*.

The author achieves his stated aim of covering concisely and practically the field of local analgesia. His use of the adjective "modern" in the latter connection is not strictly accurate. Confirmation of this is found in almost every other page. For example, neither lignocaine, amethocaine, nor hyaluronidase is included, and one looks in vain for methods of blocking the stellate ganglion. However, the book is intended as a description of the author's personal methods, and those already experienced with this form of analgesia will no doubt be interested in the outcome of Mr. Bankoff's long experience. The book is likely to be of more use to surgeons than to anaesthetists, since many of the methods described involve infiltration, as an essential part. Candidates for anaesthetic examinations may like to use this book for quick revision, but they would be well advised to distinguish carefully between Mr. Bankoff's methods, so reminiscent of those in Braun's time three or four decades ago, and those more commonly employed by anaesthetists in this country now. The illustrations are adequate and short lists of references are given at the end of each chapter. The book, though good value as far as it goes, simply cannot compare with the many excellently written and beautifully illustrated monographs on local analgesia that have appeared since the end of the war.

W. W. Mushin

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